Evaluation of the Implementation of Guidelines on the Treatment of Osteoporosis in Patients with Rheumatoid Arthritis

Sandrine Malochet-Guinamand, Céline Lambert, Laure Gossec, Martin Soubrier, and Maxime Dougados

ABSTRACT. ***Objective.*** To assess whether the 2003 and 2014 French guidelines on the prevention and treatment of glucocorticoid-induced osteoporosis (GIOP) and the 2012 update of the French guidelines for the treatment of postmenopausal osteoporosis (PMOP) were applied in patients with rheumatoid arthritis (RA).

Methods. We conducted a cross-sectional study of 776 patients with RA (19 centers). We collected the data required for the application of the various recommendations (age, sex, prednisone intake, low-energy fracture, history in the immediate family of hip fractures, and bone densitometry), anti-osteoporotic drugs, and the various factors that may be associated with the application of the recommendations.

Results. Of the patients who should have received antiosteoporosis treatment, there were 22.6% actually treated (according to the 2014 guidelines), 27.3% actually treated according to the 2003 guidelines, and of postmenopausal women, 23.6% (according to the 2012 PMOP guidelines). Applying the 2014 GIOP guidelines increased the theoretical number of patients requiring treatment relative to the 2003 GIOP guidelines (77% vs 53%; $p < 0.001$). In multivariate analysis, being treated was associated with a spinal T score ≤ –2 SD according to the 2014 guidelines; with not taking part in physical activity for more than 30 min a day according to the 2003 guidelines; and with older age, lower body mass index, and a T score ≤ –2.5 SD in at least 1 site according to the PMOP guidelines.

Conclusion. Patients with RA had inadequate prevention of GIOP and PMOP. The management of osteoporosis needs to be improved in this population. (J Rheumatol First Release August 1 2019; doi:10.3899/jrheum.180889)

Key Indexing Terms:
OSTEOPOROSIS RHEUMATOID ARTHRITIS PRACTICE GUIDELINES

Patients with rheumatoid arthritis (RA) have an increased risk of osteoporosis[1,2] and fracture[2,3,4]. The fracture risk is practically double in men and women with RA and both the spine and femoral regions can be affected[5]. This increase of fracture risk may be due to the disease itself, in particular to its activity[3], as well as its duration[6]. Debate surrounds whether corticosteroids cause bone damage when they are used to manage inflammatory diseases. Indeed, they may have a beneficial effect since they control inflammation, especially at the beginning of the disease and over short periods[7,8]. In the ESPOIR cohort of early arthritis, analysis at 7 years did not show any increase in the fracture risk from the use of low doses of glucocorticoids (GC)[9]. Prolonged GC treatment, on the other hand, seems to have a harmful effect[10,11] and appears to be an independent risk factor for fracture in RA[3].

Since the advent of biological treatments in the management of RA, the prevalence of longterm GC has dropped. The COmorbidities, EDucation in Rheumatoid Arthritis (COMEDRA) trial was a randomized multicenter study that investigated the effect of a nurse-led assessment of comorbidities and a patient self-assessment of disease activity on the management of RA. In that study, 38% of patients were receiving GC at the time of the inclusion visit[12]. Despite the availability of specific guidelines, the prevention

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of GC-induced osteoporosis (GIOP) is inadequate[13–19]. At the time of the inclusion visit of the COMEDRA cohort, only 16.8% of the patients were receiving antiosteoporosis treatment[12]. A study based on the national health insurance database of France's social security system revealed that only 12% of patients treated with prednisone received bisphosphonate treatment[20].

In 2014, updated recommendations on the prevention and treatment of GIOP (GIOP 2014) were published by the Bone Section of the French Society for Rheumatology and the Osteoporosis Research and Information Group[21]. Previous guidelines on the pharmacological treatment of GIOP had been published in 2003 (GIOP 2003) by the French Health Products Safety Agency[22]. Additionally, the updated French guidelines for the pharmacological treatment of postmenopausal osteoporosis (PMOP) were published in 2012 (PMOP 2012)[23].

The COMEDRA study was extended to 36 months to reassess the comorbidities and the utility of a standardized followup center in the management of RA. This ancillary study aimed to assess the application of the 2014 and 2003 GIOP guidelines to RA patients receiving GC as well as that of the 2012 PMOP guidelines to postmenopausal women receiving or not receiving GC.

MATERIALS AND METHODS

Population studied. This study was a posthoc analysis of the COMEDRA study (ClinicalTrials.gov: NCT01315652). COMEDRA was a French multicenter study on the assessment of comorbidities in RA and self-assessment of disease activity[12]. Twenty centers participated in the study (secondary- and/or tertiary-care French rheumatology departments), and 19 recruited patients. We included patients who took part in the study visit at Month 36 (M36).

We conducted this study at the M36 visit because comorbidities were collected for all the patients, which was not the case during the initial M0 visit.

To investigate the application of the GIOP guidelines, we included patients who received GC during the 3 months preceding the visit at M36. Each patient gave his/her free, informed consent to participate, and French authorities approved the study protocol [ethics approval: Ile-de-France III Ethics Committee, file #4-11 (B110057-30)].

Data collected. We collected the patients' general characteristics (level of education, age, sex, weight, height); current treatments including biologic agents, nonsteroidal antiinflammatory drugs taken during the previous 3 months, GC (current dose, mean dose over previous 3 mos and estimated cumulated dose at M36 since the visit at M6), and current antiosteoporotic drugs at M36 (bisphosphonates, strontium ranelate, teriparatide, raloxifene, denosumab). Also recorded were comorbidities including chronic lung disease; previous cancer (breast, prostate); history of diabetes; current or previous cigarette smoking, cardiovascular disease, and kidney failure; physical activity [for > 30 min a day (yes/no)]; and disease activity including a general assessment of the patient along with the Health Assessment Questionnaire, 28-joint count Disease Activity Score using erythrocyte sedimentation rate (DAS28-ESR) and C-reactive protein (DAS28-CRP), Clinical Disease Activity Index, and Simplified Disease Activity Index.

We also collected any previous personal history of fractures from low-level trauma including severe fractures (of the upper extremity of the femur, vertebrae, distal femur, upper extremity of the humerus, pelvis, proximal tibia, or 3 ribs simultaneously) and non-severe (other) fractures; T score (at the femoral neck, total hip, and spine); previous history in the immediate family of hip fractures; and secondary osteoporosis (due to hypogonadism, diabetes, hyperthyroidism, menopause before the age of 45, or alcohol consumption). We took bone densitometry data into account regardless of how old it was. If a number of examinations was performed, we took the most recent into account. Last, the World Health Organization fracture risk assessment tool (FRAX) score was calculated. Adjusted FRAX was calculated for the daily GC dose if it was < 2.5 mg or ≥ 7.5 mg of prednisone-equivalent[21]. The adjustment coefficient is 0.8 for a daily dose < 2.5 mg and 1.15 for a dose ≥ 7.5 mg.

Guidelines. According to the 2003 GIOP guidelines, bisphosphonate treatment is recommended for at-risk postmenopausal women, that is, for those with a history of osteoporotic fracture. If they have no history of fractures, and if the dose of GC exceeds an equivalent of 7.5 mg of prednisone, the treatment threshold is a spine or femoral neck T score < –1.5 SD. In nonmenopausal women and men, bisphosphonate treatment is initiated if the T score at one of the sites is ≤ –1.5 SD[22].

According to the 2014 GIOP guidelines, for patients receiving GC for > 3 months or beginning treatment for an expected period of > 3 months, the choice to initiate antiosteoporotic treatment is made with the aid of a decision tree that includes the patient's sex, age, menopausal status, corticosteroid dose, T score, history of fractures from low-level trauma, and adjusted FRAX score[21]. Bisphosphonates and teriparatide only were considered antiosteoporotic drugs in this population.

Finally, according to the 2012 update of the PMOP guidelines, treatment is indicated if a severe fracture occurs regardless of T score, or if a minor fracture or no fracture occurs but the T score is below the threshold of –3 SD. In other cases, the decision to treat is made with the aid of the FRAX score, in which the treatment threshold varies according to age[23]. The treatments included bisphosphonates, raloxifene, denosumab, and strontium ranelate.

Statistics. Statistical analysis was performed using Stata software (version 13; StataCorp). All tests were 2-sided, with a Type I error set at 0.05. Continuous data were expressed as mean ± SD or as median with interquartile range (IQR), and categorical variables as frequencies and associated percentages. According to 3 guidelines (2014 GIOP, 2003 GIOP, and 2012 PMOP), the number of patients who were treated among those who should have received a treatment was expressed as percentages with 95% CI. Concordance between the 2 guidelines for the management of GIOP was assessed with percent agreement and Cohen's κ coefficient. For the different guidelines, comparisons of treated and nontreated patients were performed using mixed models to take into account center as random-effect (to measure between- and within-center variability): linear mixed models for quantitative variables [e.g., age or body mass index (BMI)] and generalized linear mixed models with logit link function for binary variables (e.g., sex or medical history). Multivariate analyses were then performed considering covariates determined according to univariate results and clinical relevance (avoiding multicollinearity). The results were expressed as OR and 95% CI.

RESULTS

Altogether, 776 patients were included in the COMEDRA study extended to 3 years. They were seen between May 2014 and October 2015. Some 244 patients received GC during the 3 months preceding the M36 visit.

Application of 2014 GIOP guidelines. The application of the 2014 guidelines was studied only in postmenopausal women and elderly men (> 50 yrs) because in the other settings, treatment is not automatically given and requires an individual risk assessment. The guidelines were applied to 187 patients for whom the necessary data were available (Figure 1). The characteristics of the population are shown in Table 1.

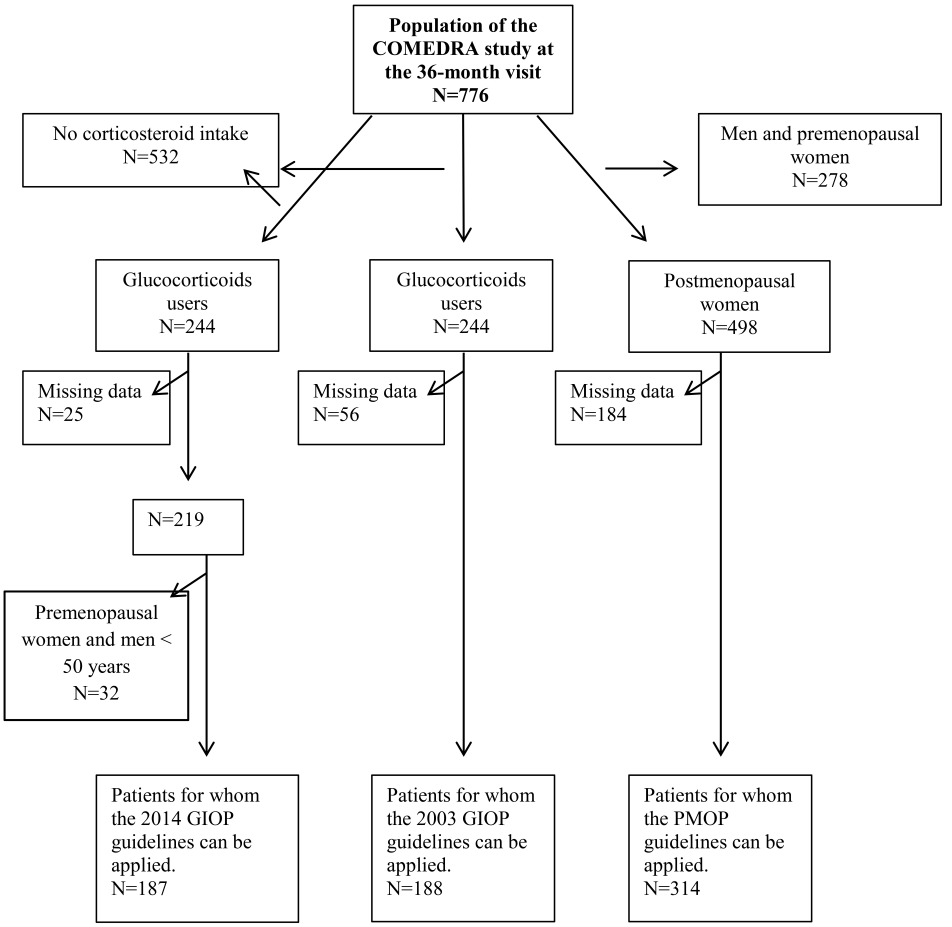

Figure 1. Flow diagram of the 3 populations studied (patients for whom the 2014 GIOP guidelines can be applied, patients for whom the 2003 GIOP guidelines can be applied, and patients for whom the PMOP guidelines can be applied). GIOP: glucocorticoid-induced osteoporosis; PMOP: postmenopausal osteoporosis; COMEDRA: COmorbidities, EDucation in Rheumatoid Arthritis trial.

Table 1. Characteristics of the 3 populations and application of guidelines.

Characteristics	Patients for Whom the 2014 GIOP Guidelines Can Be Applied, n = 187	Patients for Whom the 2003 GIOP Guidelines Can Be Applied, n = 188	Patients for Whom the PMOP Guidelines Can Be Applied, n = 314
Age, yrs	65.8 ± 8.2	63.4 ± 9.8	65.1 ± 7.9
Sex, female	153 (81.8)	160 (85.1)	314 (100.0)
BMI, kg/m^2	25.6 ± 5.1	25.3 ± 5.0	25.1 ± 4.8
RA duration, yrs	20.4 ± 10.5	20.3 ± 10.2	19.4 ± 10.3
DAS28-ESR score	3.2 ± 1.2	3.1 ± 1.2	2.8 ± 1.3
Biologic agents	147 (78.6)	148 (78.7)	242 (77.1)
Prednisone equivalent last 3 mos, mg/day	5 (3–5)	5 (2–5)	0 (0–3)
Prior fracture	84 (44.9)	81 (43.1)	114 (36.3)
Osteoporosis	40/157 (25.5)	43/174 (24.7)	76/299 (25.4)
Patients requiring treatment	164 (87.7)	99 (52.7)	212 (67.5)
Patients actually treated	39 (20.9)	39 (20.7)	57 (18.2)
Proportion of patients treated among those requiring treatment	37/164 (22.6)	27/99 (27.3)	50/212 (23.6)

Values are frequencies (%), mean ± SD, or median (interquartile range). GIOP: glucocorticoid-induced osteoporosis; PMOP: postmenopausal osteoporosis; BMI: body mass index; DAS28-ESR: 28-joint count Disease Activity Score using erythrocyte sedimentation rate; RA: rheumatoid arthritis.

Some 44.9% of the patients had a history of fractures from low-level trauma. T score data were available for 157 patients and 25.5% of them were osteoporotic with a T score ≤ –2.5 SD in at least 1 site.

Thirty-nine of 187 patients (20.9%) were receiving anti-osteoporosis treatment whereas 164 (87.7%) needed it. Two among treated patients did not actually require treatment, according to the guidelines. Only 22.6% of the patients who should have been treated if the guidelines were applied actually were treated. All the patients received bisphosphonates.

Application of 2003 GIOP guidelines. The application of the 2003 guidelines was studied in 188 patients for whom the necessary data were available (Figure 1). The characteristics of the population are shown in Table 1.

Some 43.1% of the patients had a history of fractures from low-level trauma. T score data were available for 174 patients and 24.7% of them were osteoporotic with a T-score ≤ –2.5 SD in at least 1 site.

Overall, 39 of 188 patients (20.7%) were treated with bisphosphonates as opposed to 99 (52.7%) who should have been. Twelve among treated patients did not actually require treatment according to the guidelines. Only 27.3% of the patients who should have been treated if the guidelines were applied actually were treated.

Application of 2012 PMOP guidelines. The application of these guidelines was examined in 314 postmenopausal women receiving or not receiving corticosteroids for whom the necessary data were available (Figure 1). The characteristics of the population are shown in Table 1.

There were 36.3% of the patients who had a history of fractures from low-level trauma. T score data were available for 299 patients and 25.4% of them were osteoporotic with a T score ≤ –2.5 SD in at least 1 site.

In total, 57 of 314 patients (18.2%) were receiving anti-osteoporosis treatment as opposed to 212 (67.5%) who should have received it. Seven among the treated patients did not actually require treatment, according to the guidelines. Thus, only 23.6% of the patients who should have been treated if the guidelines were applied actually were treated. The treatment was bisphosphonates in 51 cases, denosumab in 5 cases, and strontium ranelate in 1 case.

Comparison of the 2 guidelines for the management of GIOP. The 2 sets of guidelines were applicable to 185 patients. According to the 2003 guidelines, 53% of the patients should have been treated as against 77% according to the 2014 guidelines ($p < 0.001$). The percent agreement was 60%, while the κ coefficient was 0.17, indicating poor agreement.

Factors associated with treatment for the 2014 GIOP guidelines. Altogether, 164 patients should in theory have been treated according to the 2014 GIOP guidelines. Of these patients, we compared the characteristics of those who were treated against the characteristics of those who were not (Table 2).

We found that treated patients weighed less than nontreated patients (61.4 ± 10.6 kg vs 67.4 ± 15.6 kg; $p = 0.04$).

Treated patients had a lower spinal T score [–1.9 (IQR –2.5, –0.8] SD vs –1.2 (IQR –1.9, –0.3) SD; $p = 0.04$] and femoral neck T score [–2.1 (IQR –2.6, –1.7) SD vs –1.7 (IQR –2.2, –1.1) SD; $p = 0.02$]. Compared to nontreated patients, treated patients had a higher FRAX score for major fracture at 10 years without adjustment for corticosteroids (21.4 ± 17.5 vs 15.2 ± 11.3; $p = 0.02$), as well as a higher adjusted FRAX score (20.6 ± 16.9 vs 15.1 ± 11.5; $p = 0.03$).

In multivariate analysis, only spinal T score ≤ –2 was associated with a higher probability of receiving treatment (OR 3.37, 95% CI 1.12–10.10; $p = 0.03$; Figure 2A).

Factors associated with treatment for the 2003 GIOP guidelines. Altogether, 99 patients should in theory have been treated according to the 2003 GIOP guidelines. Of these patients, we compared the characteristics of those who were treated against the characteristics of those who were not (Table 3).

Fewer treated patients took part in physical activity (40.7% vs 61.1%; $p = 0.03$). Only femoral neck T score was significantly lower in treated patients than in nontreated patients [–2.2 (IQR –2.6, –1.8] vs –1.9 (–2.3, –1.4); $p = 0.03$].

Treated patients had higher adjusted and unadjusted FRAX scores than nontreated patients (unadjusted FRAX 23.6 ± 19.2 vs 16.1 ± 12.3, $p = 0.03$; and adjusted FRAX 23.3 ± 18.4 vs 15.9 ± 12.4, $p = 0.02$).

In multivariate analysis, physical activity daily was inversely associated with being treated (OR 0.11, 95% CI 0.02–0.56; $p = 0.007$). We also observed a nonsignificant trend toward an association between the probability of being treated and GC dose at M36 (OR 1.25, 95% CI 0.99–1.57; $p = 0.052$; Figure 2B).

Factors associated with treatment for the PMOP guidelines. Altogether, 212 patients should in theory have been treated according to the 2012 guidelines. Of these patients, we compared the characteristics of those who were treated against the characteristics of those who were not (Table 4).

Compared to nontreated patients, treated patients were older (68.2 ± 8.7 yrs vs 65.4 ± 7.5 yrs, $p = 0.03$) and had a lower BMI (23.2 ± 3.9 vs 24.9 ± 4.5, $p = 0.02$). They were also more likely to have osteoporosis, that is, a T score ≤ –2.5 SD in at least 1 site (59.1% vs 30.7%; $p = 0.001$) than they were to have a T score ≤ –3 SD in at least 1 site (44.1% vs 20.4%; $p = 0.006$).

Treated patients had higher unadjusted (23.2 ± 14.7 vs 16.3 ± 10.8; $p = 0.002$) and adjusted (20.4 ± 14.2 vs 14.2 ± 9.8; $p = 0.002$) FRAX scores than nontreated patients.

In multivariate analysis, age was significantly associated with receiving treatment (OR 1.06, 95% CI 1.01–1.12; $p = 0.04$), whereas BMI was inversely associated with it (OR 0.87, 95% CI 0.78–0.97; $p = 0.01$). Being osteoporotic increased the probability of receiving treatment (OR 2.42, 95% CI 1.04–5.59; $p = 0.04$; Figure 2C).

Table 2. Characteristics of the patients who should in theory have been treated according to the 2014 GIOP guidelines and comparison of the patients who were actually treated against those who were not.

Characteristics	Total, n = 164	No Treatment, n = 127	Treatment, n = 37	p
Age, yrs	66.3 ± 8.4	66.0 ± 8.3	67.2 ± 8.8	0.46
Age ≥ 70 yrs	61 (37.2)	46 (36.2)	15 (40.5)	0.56
Sex, female	134 (81.7)	102 (80.3)	32 (86.5)	0.49
Higher education	41 (25.0)	34 (26.8)	7 (18.9)	0.41
Weight, kg	66.0 ± 14.8	67.4 ± 15.6	61.4 ± 10.6	0.04
BMI, kg/m^2	25.0 ± 4.5	25.3 ± 4.7	23.7 ± 3.7	0.06
BMI < 19 kg/m^2	9 (5.5)	7 (5.5)	2 (5.4)	0.96
RA duration, yrs	20.3 ± 10.6	19.5 ± 10.2	23.0 ± 11.8	0.046
DAS28-ESR score	3.2 ± 1.3	3.3 ± 1.3	3.1 ± 1.2	0.73
DAS28-CRP score	3.1 ± 1.1	3.2 ± 0.2	2.9 ± 1.0	0.34
SDAI score	11.3 (5.3–18.6)	12.0 (5.6–19.7)	9.4 (5.3–14.9)	0.30
CDAI score	11.0 (5.0–18.0)	11.0 (5.0–19.0)	9.0 (5.0–14.0)	0.33
HAQ score	0.50 (0.12–0.87)	0.50 (0.12–0.87)	0.25 (0.00–1.00)	0.69
Physical activity ≥ 30 min/day	96/163 (58.9)	78/126 (61.9)	18 (48.6)	0.12
Renal failure	21/157 (13.4)	21/122 (17.2)	0/35 (0.0)	0.004
Current or past smoking	25 (15.2)	21 (16.5)	4 (10.8)	0.67
No. comorbidities	1 (0–1)	1 (0–1)	1 (0–1)	0.41
≥ 1 comorbidity	85 (51.8)	66 (52.0)	19 (51.4)	0.91
Current prednisone, mg/day	5 (3–5)	5 (3–5)	5 (3–6)	0.97
Current prednisone ≥ 7.5 mg/day	26/163 (16.0)	19/126 (15.1)	7 (18.9)	0.67
Prednisone equivalent since M6, mg	4390 (2732–6040)	4380 (2500–5970)	4500 (3345–6375)	0.83
NSAID	53 (32.3)	45 (35.4)	8 (21.6)	0.11
Biologic agents*	130 (79.3)	101 (79.5)	29 (78.4)	0.77
Prior fracture	84 (51.2)	60 (47.2)	24 (64.9)	0.08
Lumbar spine T score	–1.4 (–2.1 to –0.5)	–1.2 (–1.9 to –0.3)	–1.9 (–2.5 to –0.8)	0.04
Femoral neck T score	–1.8 (–2.3 to –1.2)	–1.7 (–2.2 to –1.1)	–2.1 (–2.6 to –1.7)	0.02
Femoral T score	–1.5 (–2.0 to –0.8)	–1.4 (–2.0 to –0.8)	–1.6 (–2.2 to –1.2)	0.91
At least 1 T score ≤ –1.5	97/134 (72.4)	70/101 (69.3)	27/33 (81.8)	0.26
At least 1 T score ≤ –2.5	40/134 (29.9)	26/101 (25.7)	14/33 (42.4)	0.11
FRAX, unadjusted	16.7 ± 13.2	15.2 ± 11.3	21.4 ± 17.5	0.02
FRAX, adjusted	16.3 ± 13.1	15.1 ± 11.5	20.6 ± 16.9	0.03

Values are frequencies (%), mean ± SD, or median (interquartile range). * Biologic agents: TNF inhibitor, abatacept, rituximab, or tocilizumab. GIOP: glucocorticoid-induced osteoporosis; BMI: body mass index; RA: rheumatoid arthritis; CDAI: clinical disease activity index; SDAI: Simple Disease Activity Index; HAQ: Health Assessment Questionnaire; DAS28-CRP: 28-joint count Disease Activity Score using C-reactive protein; DAS28-ESR: DAS28 using erythrocyte sedimentation rate; M6: Month 6; NSAID: nonsteroidal antiinflammatory drugs; FRAX: World Health Organization fracture risk assessment tool; TNF: tumor necrosis factor.

DISCUSSION

To our knowledge, this is the first study in France to investigate the application of guidelines on the management of osteoporosis to patients with RA.

It reveals a discrepancy between the percentage of patients with RA taking GC who should receive antiosteoporotic treatment and the percentage of those who actually do. Indeed, only 22.6% and 27.3% of patients who needed treatment were actually treated, depending on whether we applied the 2014 or 2003 guidelines, respectively.

It was perhaps a little too early to study the application of the 2014 GIOP guidelines, because they were published in October 2014 and the patients were seen for the M36 visit between May 2014 and October 2015. That said, these guidelines had been made public earlier, including at the congress of the French Society for Rheumatology in December 2013. It is also possible that the 2014 guidelines have a certain complexity that hinders their application. However, the 2003 guidelines are simpler, and they do not appear to have been applied to more patients. This inconsistency in the application of guidelines has been frequently reported in the literature. For example, it has already been shown that the guidelines on the management of osteoporosis in patients with RA have been inadequately applied[10,24,25], and that a divergence exists in cases of early inflammatory arthritis between the number of patients receiving corticosteroids who have a high risk of fracture and the number of patients treated with bisphosphonates[17,26]. Generally speaking, inadequate prevention of GIOP has been observed regardless of the underlying pathology[13,14,15,18,20].

Applying the 2014 guidelines would mean treating 23.7% more patients than by applying the 2003 guidelines. This difference may be partly due to the greater number of risk factors incorporated into the decision tree in the new guidelines, as well as to the lack of any threshold for including GC. The aim of the new guidelines was to improve the

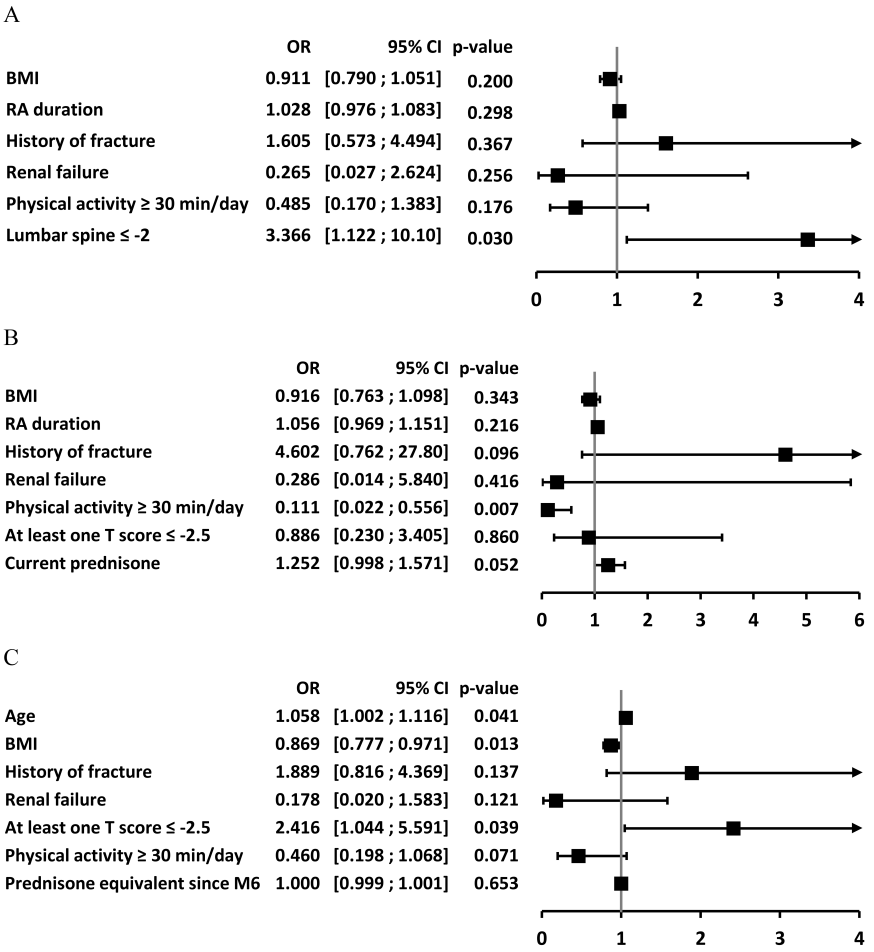

Figure 2. Multivariate analysis of the factors associated with receiving treatment according to the 2014 GIOP guidelines (A), the 2003 GIOP guidelines (B), and the 2012 PMOP guidelines (C). GIOP: glucocorticoid-induced osteoporosis; PMOP: postmenopausal osteoporosis; RA: rheumatoid arthritis; BMI: body mass index.

management of patients with GIOP[21], and indeed some studies have shown an improvement in the management of osteoporosis after guidelines were established for patients with RA[27] or for patients receiving GC[15].

In our study, the management of PMOP also appeared inadequate, because only 23.6% of women who should have been treated according to the 2012 guidelines actually were treated. This too is consistent with data published in both primary[28] and secondary prevention[28,29,30,31].

The patients treated in our study were probably the most at risk because their FRAX scores were higher than those of nontreated patients. For Watt and colleagues, even if the prevention of osteoporosis is inadequate among patients with RA, the patients with the highest FRAX scores are the ones treated[24]. However, other studies have not found this association[25,26].

In the patients in whom we studied the application of the 2003 guidelines, we observed a trend in multivariate analysis toward an association between a higher current dose of corticosteroids and treatment. The risk of fracture increases once the daily dose of GC reaches 5 mg[32].

In our study, when we considered the population to which the 2014 guidelines were applicable, a spinal T score of ≤ –2 SD was the only factor associated with being treated on multivariate analysis (OR 3.37). Similarly, in the patients in whom we studied the application of the 2012 PMOP guidelines, densitometric osteoporosis was also associated with receiving treatment on multivariate analysis (OR 2.42). It would seem that bone density remains the determining factor when deciding on initiating treatment.

In the population in which we studied the 2003 GIOP guidelines, patients who took part in regular physical activity were less likely to be treated. Older age and lower BMI were associated with a greater probability of being treated, but only in the 2012 PMOP study population. Surprisingly, we did not uncover any association between antiosteoporosis treatment and the patient's sex or history of fractures. A number of studies have shown that these risk factors influence the

Table 3. Characteristics of the patients who should in theory have been treated according to the 2003 GIOP guidelines and comparison of the patients who were actually treated against those who were not.

Characteristics	Total, n = 99	No Treatment, n = 72	Treatment, n = 27	p
Age, yrs	64.2 ± 10.9	63.5 ± 11.2	66.1 ± 10.1	0.21
Sex, female	84 (84.8)	60 (83.3)	24 (88.9)	0.54
Higher education	22 (22.2)	15 (20.8)	7 (25.9)	0.45
Weight, kg	64.4 ± 12.9	65.4 ± 13.4	61.7 ± 11.3	0.32
BMI, kg/m^2	24.6 ± 4.5	24.9 ± 4.6	23.8 ± 4.0	0.38
BMI < 19 kg/m^2	6 (6.1)	4 (5.6)	2 (7.4)	0.77
RA duration, yrs	20.2 ± 10.1	18.7 ± 9.0	24.4 ± 11.9	0.008
DAS28-ESR score	3.3 ± 1.4	3.3 ± 1.4	3.2 ± 1.4	0.79
DAS28-CRP score	3.2 ± 1.2	3.3 ± 1.2	3.1 ± 1.2	0.80
SDAI score	12.4 (5.1–19.5)	12.9 (5.1–21.1)	9.6 (5.2–17.7)	0.91
CDAI score	12.0 (5.0–18.0)	12.0 (5.0–20.0)	10.0 (5.0–17.0)	0.93
HAQ score	0.62 (0.12–0.87)	0.62 (0.25–0.87)	0.25 (0.00–1.00)	0.87
Physical activity ≥ 30 min/day	55 (55.6)	44 (61.1)	11 (40.7)	0.03
Renal failure	7/95 (7.4)	11/70 (10.0)	0/25 (0.0)	0.18
Current or past smoking	13 (13.1)	10 (13.9)	3 (11.1)	0.95
No. comorbidities	0 (0–1)	0 (0–1)	1 (0–1)	0.73
≥ 1 comorbidity	47 (47.5)	32 (44.4)	15 (55.6)	0.10
Current prednisone, mg/day	5 (3–6)	4 (2–5.5)	5 (4–7)	0.19
Current prednisone ≥ 7.5 mg/day	18 (18.2)	12 (16.7)	6 (22.2)	0.40
Prednisone equivalent since M6, mg	4324 (2760–6300)	4267 (2450–5874)	5400 (3570–6455)	0.17
NSAID	28 (28.3)	23 (31.9)	5 (18.5)	0.21
Biologic agents*	83 (83.8)	60 (83.3)	23 (85.2)	0.92
Prior fracture	77 (77.8)	53 (73.6)	24 (88.9)	0.08
Lumbar spine T score	–1.8 (–2.3 to –0.8)	–1.6 (–2.2 to –1.0)	–1.9 (–2.4 to –0.7)	0.72
Femoral neck T score	–1.9 (–2.4 to –1.6)	–1.9 (–2.3 to –1.4)	–2.2 (–2.6 to –1.8)	0.03
Femoral T score	–1.6 (–2.3 to –1.2)	–1.5 (–2.1 to –1.2)	–1.7 (–2.5 to –1.4)	0.65
At least 1 T score ≤ –1.5	78/85 (91.8)	55/61 (90.2)	23/24 (95.8)	0.52
At least 1 T score ≤ –2.5	30/85 (35.3)	21/61 (34.4)	9/24 (37.5)	0.80
FRAX, unadjusted	18.3 ± 14.9	16.1 ± 12.3	23.6 ± 19.2	0.03
FRAX, adjusted	18.1 ± 14.7	15.9 ± 12.4	23.3 ± 18.4	0.02

Values are frequencies (%), mean ± SD, or median (interquartile range). * Biologic agents: TNF inhibitor, abatacept, rituximab, or tocilizumab. GIOP: glucocorticoid-induced osteoporosis; BMI: body mass index; RA: rheumatoid arthritis; CDAI: clinical disease activity index; DAS28-CRP: 28-joint count Disease Activity Score using C-reactive protein; DAS28-ESR: DAS28 using erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; M6: Month 6; NSAID: nonsteroidal antiinflammatory drugs; SDAI: Simple Disease Activity Index; FRAX: World Health Organization fracture risk assessment tool; TNF: tumor necrosis factor.

likelihood of being prescribed preventive treatment for GIOP, for instance female sex[13,15,17,20], menopausal status[13,25], and age[20,25]. Conversely, male sex can lower the chances of being treated[19].

Moreover, we did not find any link between treatment and the comorbidities. This is despite a certain number of studies revealing a reduced probability of antiosteoporosis treatment in patients with a high number of comorbidities[33,34].

Some studies have shown that the initiation of preventive treatment for GIOP depended on the practitioner examining the patient[13,15]. In our study we do not know who initiated the antiosteoporosis treatment. Given that the patients were participating in a study that evaluated comorbidities, one might have thought that this would have increased the proportion of patients whose osteoporosis was treated. Indeed, during the M6 visit of the COMEDRA study, the patients who underwent a nurse-led comorbidity assessment were more likely to receive antiosteoporosis treatment. The mean (± SD) number of measures (dual-energy x-ray absorptiometry scan, initiation of osteoporosis therapy, vitamin D or calcium supplementation, increased calcium intake, increased physical activity) taken in the comorbidity group was 1.08 (± 0.99) versus 0.31 (± 0.55; p < 0.001) in the self-assessment group, with an incidence rate ratio of 3.45 (95% CI 2.91–4.09)[12]. A qualitative survey of family physicians on the prevention of GIOP uncovered a certain number of barriers to treatment, specifically a lack of knowledge, lack of time, issues with patient adherence, and problems arising from the healthcare system[18].

Our study has certain strengths, such as its relatively exhaustive collection of osteoporotic risk factors, comorbidities, treatments, fractures, and bone densitometry results to assess the number of patients requiring treatment according to the different guidelines.

The present study has certain limitations, for instance, a certain amount of missing data on corticosteroid use, menopausal status, and T score. It does not investigate the barriers behind the low proportion of patients receiving

Table 4. Characteristics of the patients who should in theory have been treated according to the 2012 PMOP guidelines and comparison of the patients who were actually treated against those who were not.

Characteristics	Total, n = 212	No Treatment, n = 162	Treatment, n = 50	p
Age, yrs	66.0 ± 7.9	65.4 ± 7.5	68.2 ± 8.7	0.03
Higher education	63 (29.7)	50 (30.9)	13 (26.0)	0.64
Weight, kg	62.1 ± 11.4	63.4 ± 11.9	58.1 ± 8.6	0.004
BMI, kg/m^2	24.5 ± 4.4	24.9 ± 4.5	23.2 ± 3.9	0.02
BMI < 19 kg/m^2	14 (6.6)	9 (5.6)	5 (10.0)	0.20
RA duration, yrs	20.8 ± 10.3	19.8 ± 9.4	24.2 ± 12.4	0.008
DAS28-ESR score	2.9 ± 1.3	2.9 ± 1.3	2.8 ± 1.3	0.84
DAS28-CRP score	2.8 ± 1.1	2.7 ± 1.1	2.8 ± 1.1	0.80
SDAI score	7.5 (4.1–14.1)	7.2 (4.1–14.1)	9.0 (3.1–14.1)	0.87
CDAI score	7.0 (4.0–13.0)	7.0 (4.0–13.0)	9.0 (2.5–13.5)	0.72
HAQ score	0.25 (0.00–0.75)	0.25 (0.00–0.62)	0.37 (0.00–0.75)	0.17
Physical activity ≥ 30 min/day	130 (61.3)	104 (64.2)	26 (52.0)	0.17
Renal failure	21/209 (10.0)	20/160 (12.5)	1/49 (2.0)	0.07
No. comorbidities	0 (0–1)	0 (0–1)	0 (0–1)	0.46
≥ 1 comorbidity	102 (48.1)	79 (48.8)	23 (46.0)	0.99
Current prednisone, mg/day	0 (0–4)	0 (0–4)	0 (0–4)	0.64
Prednisone equivalent since M6, mg	240 (0–3625)	210 (0–3430)	940 (0–4080)	0.60
NSAID	51 (24.1)	43 (26.5)	8 (16.0)	0.16
Biologic agents*	168 (79.2)	130 (80.2)	38 (76.0)	0.23
Prior fracture	99 (46.7)	69 (42.6)	30 (60.0)	0.06
Lumbar spine T score	–1.4 (–2.3 to –0.6)	–1.3 (–2.2 to –0.5)	–2.2 (–3.0 to –1.1)	0.003
Femoral neck T score	–1.9 (–2.4 to –1.5)	–1.8 (–2.3 to –1.3)	–2.2 (–2.9 to –1.9)	0.001
Femoral T score	–1.6 (–2.1 to –0.9)	–1.5 (–2.0 to –0.8)	–1.7 (–2.7 to –1.6)	0.07
At least 1 T score ≤ –1.5	158/197 (80.2)	118/153 (77.1)	40/44 (90.9)	0.06
At least 1 T score ≤ –2.5	73/197 (37.1)	47/153 (30.7)	26/44 (59.1)	0.001
At least 1 T score ≤ –3	45/181 (24.9)	30/147 (20.4)	15/34 (44.1)	0.006
FRAX, unadjusted	17.9 ± 12.1	16.3 ± 10.8	23.2 ± 14.7	0.002
FRAX, adjusted	15.6 ± 11.2	14.2 ± 9.8	20.4 ± 4.2	0.002

Values are frequencies (%), mean ± SD, or median (interquartile range). * Biologic agents: TNF inhibitor, abatacept, rituximab, or tocilizumab. PMOP: postmenopausal osteoporosis; BMI: body mass index; RA: rheumatoid arthritis; CDAI: clinical disease activity index; DAS28-CRP: 28-joint count Disease Activity Score using C-reactive protein; DAS28-ESR: DAS28 using erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; M6: Month 6; NSAID: nonsteroidal antiinflammatory drugs; SDAI: Simple Disease Activity Index; FRAX: World Health Organization fracture risk assessment tool; TNF: tumor necrosis factor.

treatment. Indeed, it is possible that we underestimated the proportion of patients being treated, because we did not count patients who may have discontinued their treatment before the visit at M36. On the other hand, it is also possible that we overestimated the number of patients who needed treatment, because we did not have complete records on GC treatment between M6 and M36.

This study confirms that the prevention and management of osteoporosis continues to be inadequate among patients with RA, regardless of whether they are treated with GC. Setting up nurse-led comorbidity consultations may be a solution[12]; it would be necessary to assess their longterm utility.

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