Assessment of fracture risk in patients with spondyloarthritis using the FRAX scores

Évaluation du risque de fracture chez les patients atteints de spondylarthrite en utilisant le score d'évaluation du risque de fracture (FRAX)

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RÉSUMÉ

Objectifs : Cette étude avait pour objectifs de mesurer la densité minérale osseuse (DMO), d'évaluer le score FRAX (fracture risk assessment tool) et de déterminer les facteurs associés à un risque élevé de fracture chez les patients tunisiens atteints de spondylarthrite (SA).

Méthodes: Il s'agissait d'une étude transversale prospective. Nous avons calculé le risque de fracture de la hanche (HF) et de fracture ostéoporotique majeure (MOF) sur 10 ans à l'aide de l'outil d'évaluation du risque de fracture (FRAX).

Résultats: soixante-quinze patients ont été recrutés. Le MOF était significativement associé à la perte osseuse (p = 0,000). Il était associé à l'ASDASCRP mais sans atteindre le seuil de significativité (p = 0,05). Le MOF et la FH étaient tous deux significativement associés à l'âge au début de la SA (respectivement, p = 0,003 et p = 0,002). Le risque de FH était plus élevé lorsque BASRI (p = 0,036) et la vitesse de sédimentation (VS) étaient élevés (p = 0,014), il était également associé à l'âge (p = 0,002) et à une carence en vitamine D (p = 0,043).

Conclusion: Le score MOF chez les patients atteints de SA était associé à une perte osseuse, à l'âge au début de la maladie et à l'ASDASCRP. Le score HF était associé à l'âge, à la carence en vitamine D, à l'âge au début de la maladie, au BASRI de la hanche et à la vs élevée.

Mots-clés

Spondyloarthrite, DMO, FRAX,fracture

SUMMARY

Osteoporosis and fractures are known to complicate spondyloarthritis (SA). The Fracture Risk Assessment Tool (FRAX) estimate the 10-year probability of major osteoporotic fracture (MOF) and also hip fracture (FH). It can be useful as risk assessment tools for the purpose of preventing fracture in SA. This study aimed to measure the bone mineral density (BMD), to evaluate the FRAX and to determinate factors associated with high risk of fracture in patients with SA. It's a prospective cross-sectional study that included seventy-five patients admitted for SA, in the rheumatology department of Kassab institute in Tunisia. All of them fulfilled the modified New York criteria for SA.

Results: Sixty-two men and thirteen women were enrolled, with mean age of 36.8 ± 11.8 years. The mean age at disease onset was 27.8± 9.9 years. Mean BASDAI and ASDAS CRP were respectively 3.5 ± 2.4 and 3 ± 0.83. The mean BASRI was 8.9 ± 4.2 and the mean mSASSS was 17.6 ± 19.6. Vitamin D insuffiency and deficiency were found in 43 and 30 patients respectively. Osteoporosis (T score ≤ -2,5 SD) were found in 49% of patients and 80 % of them have a reduced BMD (T score ≤ -1 SD). The mean MOF score was 0,36 ± 0,3 [0-0,9] and the mean FH score was 0,3 ± 0 [0-0,5]. The MOF was significantly associated with Bone loss (p=0.000). A trend for a significant association was also found with ASDASCRP (p=0.05). The MOF and FH were both significantly associated to the age at the onset of SA (respectively, p=0,003 and p=0,002). The risk of FH was higher when hip BASRI (p=0.036) and ESR were high (p=0,014), it's also associated to age (p=0.002) and vitamin D deficiency (p= 0.043). However, no correlation was found between the MOF and FH and the presence of peripheral arthritis, enthesitis or hip arthritis.

Conclusion: The MOF score, in patients wih SA, was associated with bone loss, age at disease onset and ASDASCRP. The HF score was associated with age, Vitamine D deficiency, age at disease onset, high hip BASRI and high ESR.

Key-words

Spondyloarthritis, BMD, FRAX, fracture

INTRODUCTION

Many studies have reported an increased risk of fracture in patients with spondyloarthritis (SA). These findings may be explained by the chronic inflammation that activates the osteoclasts (1,2). Hip and vertebral fractures lead to long-term nursing care, neurological complications, disability and can cause medico economic concerns. Therefore, predicting the factors associated with high fracture risk in SA patients is essential to prevent it. The Fracture Risk Assessment Tool (FRAX) estimate the 10-year probability of major osteoporotic fracture (MOF) and also hip fracture (FH) (3). This tool was conceived to evaluate osteoporotic risk of fracture in menopaused women, it is commonly used in RA but not in SA. Since there is no available tool adapted to the situation of osteoporotic fracture risk in SA, FRAX may be useful in this condition. The adapted version of the FRAX to Tunisian population, is available on WHO website since 2 years. Our study aimed to measure the BMD, to evaluate the FRAX and to determinate factors associated with high risk of fracture in patients with SA in a Tunisian rheumatology center.

METHODS

It's a prospective and cross-sectional study that included seventy-five patients admitted for SA, in the rheumatology department of Kassab Institute in Tunisia. All of them fulfilled the modified New York criteria for SA.

We calculated the risk of Hip Fracture (HF) and Major Osteoporotic Fracture (MOF) over 10 years using the fracture risk assessment tool (FRAX) which was recently adapted to the Tunisian population. We evaluated for each patient the different parameters related to SA as well as the risk factors for osteoporosis. We assessed bone mass of lumbar spine (anteroposterior and lateral views) and proximal femur, using DEXA (General Electric LUNAR). Results were expressed as bone mineral density (BMD in g/cm2) and T-scores. We used the WHO classification for quantifying the bone mass loss.

Patients using other treatments than those used for SA, or having an impact on bone metabolism were not included. Also we excluded patients whose clinical examination or laboratory assessment have detected a disorder that had an impact on BMD, such as endocrine disorders or osteomalacia. We used the Statistical Package for Social Sciences (SPSS) 17.0 to analyse the results.

RESULTS

Seventy-five patients were enrolled (82,6% men and 17,33 % women), with mean age of 36,8 ± 11,8 years. The mean body mass index (BMI) was 24,9 ± 4,5 kg/m², and six patients have a BMI under 19 kg/m². Eight patients consumed alcohol and 42,7 % of patients were active smokers. Two patients had a parental history of fragility femoral neck fracture.

The mean age of patients at disease onset was 27,8± 9,9 years and the mean disease duration was 9 ± 7,9 years.

The mean Bath Ankylosing Spondylitis Disease Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score ($ASDAS_{CRP}$) were respectively 3,5 ± 2,4 and 3 ± 0,83. The mean Bath Ankylosing Spondylitis Functional Index (BASFI) was 3,8 ± 2,5, the mean Bath Ankylosing Spondylitis Metrologic Index (BASMI) was 4,2 ± 2 and the mean Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) was 1,6 ± 2,4. The mean Bath Ankylosing Spondylitis Radiographic Index (BASRI) was 8.9 ± 4.2, the mean sacroiliac BASRI was 3,3 ± 0,8, the mean BASRI Hip was 1.6 ± 1.7 and the mean modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was 17.6 ± 19.6.

All patients have normal markers of calcium metabolism (mean calcaemic level was 2,33 ± 0,128 mmol/l, mean alkaline phosphatase level was 226,38 ± 28,35 U/l, and mean phosphoremia was 1,03 ± 0,33 mmol/l). Mean Vitamin D blood level was 12,8 ± 6,48 ng/ml. Vitamin D insuffiency and deficiency were found in 43 and 30 patients respectively. The mean parathyroid hormone (PTH) was 2,4 ± 1,4 pmol/ml with extremes between 0,85 and 6. Disruption in sexual hormones blood levels was found in 7 cases without clinical outcomes (two cases of hypotestosteronemia, three cases of high level of FSH and two cases of high level of LH).

The mean BMD value of lumbar anteroposterior spine was 0,658 ± 0,24 g/cm², in lateral spine it was 0,633 ±0,21 g/cm² and in total hip it was 0,933 ± 0,16 g/cm².

Considering the WHO classification, osteoporosis (T score ≤ -2,5 SD) frequency were found to be 49%, and 80 % of patient had a reduced BMD (T score ≤ -1 SD).

The mean risk of major fracture in 10 years (MOF) was 0,36 ± 0,3 with extreme [0-0,9]. The mean risk of hip fracture in 10 years (HF) was 0,3 ± 0 with extremes between 0 and 0,5.

Correlation between BMD and FRAX scores

The MOF was significantly and negatively correlated with spinal anteroposterior BMD, hip BMD, lateral spinal T score and hip T score (table 1). Concerning HF, it was negatively correlated with lateral spinal T score (p=0,024) and curiously not associated to hip BMD (table1). Furthermore, we studied the relation between the FRAX scores and the bone loss (T score ≤ -1 SD), and we found a significant association between the MOF and bone loss (p=0,03) (table2).

Table 1: Correlation between BMD and FRAX

	FRAX Major Fracture		FRAX Hip fracture	
	r	P	r	P
BMD AP	**-0,360**	**0,005**	-0,246	0,06
BMD LS	-0,178	0,178	-0,107	0,421
BMD H	**-0,424**	**0,001**	-0,199	0,13
T score AP	-0,135	0,310	-0,247	0,06
T score LS	**-0,321**	**0,013**	**-0,294**	**0,024**
T score H	**-0,333**	**0,01**	-0,08	0,548

BMD bone mineral density, BMD AP: spine BMD measured in AP view, BMD LS: BMD spine measured in lateral view, BMD H: BMD measured the hip neck.

Association between FRAX scores and risk factors of fracture in general population:

Concerning demographic parameters (age, sex) and those regarding lifestyle (smoking, alcohol and coffee consumption...), only age was positively associated to the MOF and HF, with respectively p=0,000 and p=0,002. Sexual hormones and PTH didn't have any influence in the risk of fracture.

However, the deficiency in vitamin D was found to be associated to HF (p=0,043) (table 2).

Association of FRAX scores with SA parameters:

The MOF and the HF were significantly positively associated to the age at the onset of SA (p=0,003 and p=0,002). In fact, more the disease stated late more the patient was exposed to fractures.

The risk of hip fracture was also higher when hip BASRI and ESR were high (p=0,036 and p=0,014). A trend to significant association was also found between MOF and $ASDAS_{CRP}$ (p=0.05).

However, no correlation was found between the FRAX scores and SA clinical expression (presence or not of peripheral arthritis and enthesitis), high biologic inflammatory parameters or hip arthritis (p> 0,05) (table 2).

Table 2: Association between FRAX scores and SA parameters.

	MOF		HF	
	r	P	r	P
Age	0,536	**0,00**	0,395	**0,002**
Sex		0,551		0,614
Tabaco		0.177		0.192
Coffee		0.736		0.192
Alcohol		0.636		0.612
BMI	-0.151	0.255	-0.123	0.354
Vitamin D	-0,123	0,673	-0,264	**0,043**
PTH		0,097		0,942
Sexual hormones deficiency		0,174		0,322
T score < -1DS		**0,032**		0,134
Age at disease onset	0,381	**0,003**	0,403	**0,002**
SA with peripheral arthritis		0,895		0,452
Hip arthritis		0,478		0,119
Disease duration	0,195	0,143	-0,028	0,832
BASMI	0,186	0,158	0,77	0,56
MASES	-0,012	0,94	-0,137	0,382
BASFI	0206,	0,118	0,052	0,696
BASDAI	0,164	0,214	0,1	0,449
ASDAS CRP	0,301	**0,05**	0,012	0,937
BASRI hip	0,037	0,791	0,288	**0,036**
Sacroiliac BASRI	0,245	0,077	-0,057	0,687
Total BASRI	0,174	0,189	0,172	0,193
mSASSS	0,056	0,698	-0,101	0,481
ESR	0,126	0,35	0,325	**0,014**
CRP	0,135	0,323	0,075	0,583

DISCUSSION

The bone mineral statue is modified in SA, with an increase of bone loss and a decrease of bone mineral density (4). However, the 10-year risk of fracture is not clearly assessed in patients with SA.

A recent systematic review showed that loss of bone mass complicates not only long-term SA but also early SA (5). In our study, 49% of patients had an osteoporosis, and 80 % of patient had a reduced BMD; with mean disease duration of 9 years.

A Danish nationwide study calculating the real prevalence of fracture in AS patients, identified 0.11% AS fracture cases, compared to 0.07% in controls. Unadjusted (age- and gender-matched) odds ratio (OR) were 1.54 [95% confidence interval (95%CI) 1.26-1.89] for any fracture, 5.42 [2.50-11.70] for spine and 1.39 [1.12-1.73] for non-vertebral fracture. The risk peaked in the first 2.5 years following AS diagnosis: OR 2.69 [1.84-3.92] for any fracture [6].

A Swedish study among SA patients reported that the 10-years probability of major osteoporotic and hip fracture was respectively 9.9 ± 9.7% and 2.4 ± 6.0% (7). These

values are higher than ours and that could be explained by the differences in the population characteristics of the two studies. In fact, in the Swedish study the population was made essentially by male and our female patients were premenopausal but the Swedish study included menopausal female patients. The mean age in Swedish study was 50 ± 13 years and disease onset age was 15 ± 11 years, versus 36,8 ± 11 years and 27,8 ± 9,9 years respectively in our study. Thus, these results suggest that bone loss begins early in the course of the disease but continues and worsens during the disease.

Concerning disease activity scores, many studies confirmed that the activity of the diseases is related to the bone loss. Nevertheless, the association of disease activity to the risk of fracture was not assessed in the literature. In our study we found a trend to significant correlation between ASDAS CRP and MOF FRAX [8,9].

In this current study, we found that age was a risk factor of MOF (p=0,00) and HF (p=0,002), in accordance with literature. Kanis and al reported that FRAX score increase with age (10).

Furthermore, the severity of radiographic hip arthritis was independently associated with the 10-year risk of hip fractures. Capaci and al in a study including 73 patients with SA found that more hip BASRI was higher more the BMD was lower (11). So patients with advanced SA, with severe hip arthritis are more exposed to hip fracture by bone loss; hence the need of increased awareness of hip fracture risk in SA.

Sacroiliac BASRI was not associated to the calculated risk of fracture in our study. Kang and al, who compared 240 axial SA patients to 1200 healthy controls in a Korean center using FRAX score, found that the severity of sacroiliitis was independently associated with both MOF and HF risk (12). The same study revealed that previous fracture, parental history of HF, current smoking status, and the severity of sacroiliitis were independently associated with HF risk (respectively $\beta = 0.283$, $p = 0.026$; $\beta = 0.428$, $p = 0.001$; $\beta = 0.291$, $p = 0.014$; and $\beta = 0.286$, $p = 0.020$). Multivariate analysis also showed that the severity of sacroiliitis, age, occurrence of previous fracture, and parental history of HF were independently associated with an increased 10-year probability of MOF (7).

While mSASSS is known to be correlated to the incidence of vertebral fractures [13, 14], in our study it was not associated to the 10-year probability of fracture. The association between mSASSS and the FRAX scores was not assessed in other studies. These findings allow us to conclude that probably the FRAX scores underestimates the risk of spine fracture in AS patients.

Concerning biologic parameters, vitamin D deficiency was found to be associated to the HF risk in our study. In fact, it known that high disease activity in SA is associated with an alteration of vitamin D metabolism and increased bone resorption which explains the high risk of fracture (15, 16).

Finally, our study demonstrated that FRAX scores can be useful in SA patients to predict the risk of fracture. Nevertheless, the MOF and the HP scores remain less the real risk of fracture calculated in the epidemiologic studies. Hence we suggest that the fact of including the AS as an independent parameter in the calculation of FRAX may improve the performance of this score, like what is done with the rheumatoid arthritis.

In conclusion, we have demonstrated, using the FRAX, that the risk of major and hip fracture was significately associated to the age, the disease onset, hip BASRI and ESR. The FRAX can be used as a reliable tool to evaluate the fracture risk in SA patients. Nevertheless, including the AS as an independent parameter in the calculation of FRAX may improve the performance of this score.

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