Research Article

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Comorbidities in rheumatoid arthritis: the RBSMR study

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Objective: The objectives of this study are as follows: to define the profile of comorbidities during rheumatoid arthritis; deduce the predictive factors for their occurrence and their impact on the activity and severity of the disease.
Methods: 225 patients followed for rheumatoid arthritis, meeting the ACR/EULAR 2010 criteria under biotherapy, included in the national biotherapy register. We proceeded to group patients into 2 groups: patients with and without co-morbidities in order to study the prevalence of co-morbidities, their predictors of occurrence and the correlation between these co-morbidities, the activity and the severity of the disease.
Results: The average age was 51.94 years ± 11.36 (20-80) with a female predominance of 87.6%, the average duration of evolution was 737.8 weeks with an average diagnostic delay of 719.5 weeks. The average SAR 28 (crp) was 3.5 ± 1.39. Corticosteroid therapy was noted in 94.2%, with an average cumulative dose of 37,360 mg. The average body mass index was 27.56 kg/m^2.
At least comorbidity was present in 67.1% of patients, the most common of which was osteoporosis (22.7%).
The presence of comorbidity was associated with a longer duration of development (p=0.001) and positive rheumatoid serology (p=0.049). Likewise, they were more frequent among women without a profession.
Conclusion: Our study confirms the high prevalence of comorbidities during rheumatoid arthritis, hence the importance of screening them for better management.

Keywords: rheumatoid arthritis • comorbidities • hypertension • cardiovascular disease

Introduction

Rheumatoid Arthritis (RA) is the most common chronic inflammatory rheumatism. It is a systemic disease with extra-articular manifestations causing comorbidities. Comorbidities cause not only an aggravation of the disease but also an increase in mortality and costs of care. There is therefore a real need for systematic screening of major comorbidities. The objectives of this study are to define the prevalence of comorbidities during rheumatoid arthritis and to specify their influence on the course of the disease.

Patients and methods

The observational cross-sectional observational study of 225 patients monitored for RA, meeting the ACR / EULAR 2010 criteria under biotherapy, included in the national register from a database frozen at the end of January 2019. We proceeded to the distribution of patients into 2 groups: patients with and without comorbidities to study the prevalence of comorbidities, the correlation between these comorbidities, activity and severity of the disease. Using an SPSS (Statistical Package for the Social Sciences) Version 20, an overall description of the study population and a bi Analysis and Multivariate were performed and p value <0.05 was considered significant.

Results

The average age was 51.94 ± 11.36 years (20-80) with 87.6% female, average disease duration was 737.8 weeks with an average diagnosis time of 719.5 weeks. The Disease Activity Score (DAS 28- CRP) average is 3.5 ± 1.39. The HAQ average is 1.22. Corticosteroid therapy is noted in 94.2%, with an average cumulative dose of (37360 mg). The average body mass index is 27.56 kg/m^2.

At least one comorbidity was found in 67.1% of patients, the most frequent of whom were osteoporosis (22.7%), diabetes (20.4%), hypertension (16.4%) and dyslipidemia (15.1%) (Table 1). In bi and multi-variate analysis the presence of comorbidity is associated with a longer duration of evolution (p=0.001), occupation (women without occupation, p=0.031), positive rheumatoid serology (p=0.049) (Tables 2 and 3).

The results of our study suggest that the presence of comorbidity in rheumatoid arthritis is associated with a longer duration of evolution

Table 1. Prevalence of comorbidities during RA in our series.			
Comorbidity Category	**Comorbidity**	**Number of patients**	**Percentage %**
cardiovascular disease (CV)	Arterial hypertension	37	16.4
	Systemic heart disease Treatment with anti platelet aggregators in progress	7	3.1
	1st-degree family history of coronary artery disease / cerebral vascular accident	8	3.6
Metabolic diseases	Diabetes	46	20.4
	Dyslipidemia	34	15.1
Infections	Infections		
	Viral infections: 5 cases of infection with hepatitis B virus	5	2.2
	Other hepatitis	1	0.4
	Bacterial infections:20 TB cases (13 pulmonary, lymph node 2, 1 intestinal, genital 1, 1 osteoarticular, 1 subcutaneously)	20	8.9
Gastroduodenal diseases	Gastroduodenal diseases: Peptic ulcer	7	3.1
Psychiatric diseases	Depression	12	5.3
Osteoporosis	Osteoporosis	51	22.7
Cancers	Multiple myeloma	1	0.4

Table 2. Factors associated with the presence of comorbidities in patients with RA in our series.			
Parameters	**RA with comorbidities**	**RA without comorbidities**	**P value**
Age	54.4	46.8	P= 0.54
Sex	86.1% (F) /13.9% (H)	90.5% (F) / 9.5% (H)	P=0.23
profession	78.6 %	72.20%	P=0.000
Duration of evolution (weeks)	45.6	42.9	P=0.031
diagnosis delay (Weeks)	131.6	215.2	P=0.19
Current biotherapy duration (weeks)	8.9	10.9	P=0.42
Taking steroids	95.4 %	91.90%	P=0.42
Inflammatory syndrome	22.10	25.67	P=0.21
Disease activity (DAS28 CRP)	3.55	3.63	P=0.30
Positive rheumatoid serology (FR and / or ACPA)	96.6 %	89.9 %	P=0.049
The destructive damage	91,5 %	94.4 %	P=0.37

Table 3. factors associated with the presence of comorbidities after multi varied analysis.	
Parameters	**P value**
Positive rheumatoid serology	P=0.044
Longer evolution time	P=0.002

and a positive rheumatoid serology. However, it was not associated with age, sex, diagnosis time, the inflammatory syndrome, the disease activity, to structural damage, to taking steroids and duration of current biotherapy.

Discussion

Rheumatoid Arthritis (RA) is the most common chronic inflammatory rheumatism with an average prevalence of 0.5 to 1% in developed countries [1] and 0.3 to 0.5% in developing countries [2]. The inflammation in RA is not limited to joints, it affects several vital organs (cardiovascular system, bone, lung, etc.) and is the cause of comorbidities. The latter are more frequent, more serious and less supported than in the general population. They are responsible for excess mortality [3-6].

These comorbidities are represented by cardiovascular disease (myocardial infarction, stroke) [4,6-8] cancers (breast, lung, skin, colorectal and prostate) [9]; complications

related to infections (influenza, pneumonia) [10,11] and osteoporosis (vertebral fracture, wrist fracture) [12,13].

Many studies are interested in studying the prevalence of comorbidities; This varies between 40 and 66% [14-16]. In our series, at least one comorbidity was noted in 67.1% of patients. They were listed as follows: 22.7% of osteoporosis, 20.4% of diabetes, 16.4 % of hypertension, 15.1% of dyslipidemia.

The risk of osteoporosis is multiplied by 2 in patients with RA due to the disease itself and prolonged use of corticosteroids [17,18]. Cardiovascular risk in patients with RA is related to both traditional risk factors, anti-inflammatory drug use and chronic inflammation [19,20].

It should be noted, that the published literature reports a high incidence of smoking and diabetes in RA patients, making this disease a cardiovascular risk factor established alongside conventional factors [21,22].

The risk of infection is also multiplied by 2 in patients with RA [23]. This is explained by an inherent immune-modulating the autoimmune disease; extra-articular disease, especially pulmonary, by the presence of other comorbidities such as diabetes or smoking and by treatments used with an increased risk for corticosteroids compared to targeted therapies [23]. The risk of infection primarily concerns the upper airways, lungs and urinary tract. Targeted therapies increase the risk of reactivation of latent tuberculosis, this risk is multiplied by 4 in RA [24]. Thus a systematic screening is essential before the initiation of biologicals. In our study, the risk of infection was not dominant. 9 infections It was noted by the virus of hepatitis B and 20 cases of tuberculosis have been identified (13 lungs, lymph node 2,1 intestinal, genital 1,1 osteoarticular, 1 subcutaneously), it's' probably a selection bias, since patients were eligible for biotherapy.

The prevalence of comorbidities in a Thaï study is 53.6%, of which the most common: hypertension (51.2%), dyslipidemia (34.6%), ophthalmic diseases (34.6%), the osteoporosis (19.8%) and diabetes (13.1%) [25]. In KRAC study, the prevalence of comorbidities was approximately 40% as follows: hypertension (20.7%), thyroid disease (18.3%) and diabetes (14.4%) [26].

Factors associated with comorbidities differ based on studies including advanced age of patients, prolonged DMARDs and longer diagnostic delay [25,26]. In our series, the longer duration of evolution and positive rheumatoid serology were significantly associated with the presence of comorbidities.

Although RA patients are exposed to cardiovascular risk greater than the general population, they are paradoxically less well detected [27] RA should be considered as a cardiovascular risk factor in its own right with all its consequences, not just a deforming inflammatory arthritis.

The recommendations of the European league of Rheumatology (EULAR) and the French Society of Rheumatology (SFR) highlight the role of the rheumatologist in the organization of screening and support Cardio Vascular risk of RA patients [28,29]. The 2018 update of recommendations on the management of RA insists heavily on the importance of taking care of the patient as a whole including the screening and management of comorbidities [29]. The collection and screening of comorbidities and the updating of preventive measures can be organized in different ways.

RA causes disability and premature mortality, it also causes substantial problems of health and economic to patients and their families and to the society and the nation [30,31]. In addition to the disease itself, the presence of cardiovascular disease, the most common comorbidity has led to an increase in mortality in patients with RA [32-34].

There is therefore a need to organize a systematic screening of major comorbidities and maintain preventive measures such as immunization. Some suggest that they be made by specialized nurses as in the COMORA study [35]. Others in various consultations of rheumatology or even in dedicated day of hospitalization, as is the case in Montpellier [36].

Conclusion

Patients with RA have an increased risk of developing comorbidities, exposing them to excess mortality. Their screening is currently insufficient and it is essential that the medical community become aware of these risks in order to better apprehend them. Thus screening and

periodic evaluation of comorbidities, their risk factors and their management must be achieved.

Declaration of links of interest

The authors declare that they have no links of interest.

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Ethics approval

The protocol for the original RBSMR study was reviewed and approved by local institutional review boards and the national ethic committee.

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