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Cardiovascular risk in rheumatoid arthritis – evaluation and treatment

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ABSTRACT

Introduction: Rheumatoid arthritis patients have an increased risk of cardiovascular morbidity and mortality. Consecrated cardiovascular risk management strategies are underused in this patients. The purpose of this paper is to evaluate, in rheumatoid arthritis hospitalized patients, the level of cardiovascular risk and the degree of implementation of currently recommended cardiovascular risk reduction treatments.

Materials and methods: 130 active rheumatoid arthritis patients, consecutively admitted in the Rheumatology Clinic of our hospital, were evaluated based on clinical exam, routine biochemistry, X-ray, electrocardiogram and cardiac ultrasound. We noted the characteristics of the rheumatic disease, the cardiovascular risk factors and organic heart disease. The risk for cardiac death at 10 years was estimated using the SCORE table; and adequate use of cardiovascular risk reduction therapies (antiaggregants, statin, antihypertensive medication) was checked.

Results: Organic heart disease was identified in 28.4% of the patients. The most frequent encountered risk factors were dyslipidemia (62.3%), hypertension

(54.6%) and abdominal obesity (53%). Globally, 66.1% of the patients were classified as having high cardiovascular risk. Hypertension and dyslipidemia were treated in 81.6%, respective 40.7% of the cases and controlled to recommended therapeutic goals in 70.4%, respective 22.2%. Among the patients with a symptomatic atherosclerotic disease, less than one half (48.6%) were treated with antiaggregants.

Conclusion: Organic heart disease was frequent among rheumatoid arthritis patients; the most prevalent cardiovascular risk factors were hypertension, dyslipidemia and abdominal obesity. The treatment and control rates for hypertension were acceptable, but statins and antiaggregants were grossly underused.

Keywords: rheumatoid arthritis, cardiovascular risk management, hypertension, dyslipidemia, antiaggregants

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Introduction

Rheumatoid arthritis (RA) patients are known to have an increased cardiovascular (c.v.) morbidity and mortality, particularly by coronary heart disease [1]. Subjects with high levels of disease activity and inflammation are most vulnerable [2]. The risk can be decreased by using remotive therapy and by controlling the traditional c.v. risk factors, like smoking, hypertension, dyslipidemia and diabetes. In spite of the fact that current practice guidelines present clear recommendations for c.v. risk management [3,4], preventive c.v. treatments are underused, both in the general population [5], and in RA patients [6,7].

The aim of our study was to determine, in real life unselected hospitalized RA patients, the prevalence of organic heart disease and of c.v. risk factors, the global risk of c.v. death, and the rate of preventive medication administration, where indicated.

Table I. Cardiovascular risk factors

Risk factor	Definition
Hypertension	At least two blood pressure values equal or superior to 140/90 mmHg, obtained in basal conditions; and/or anti-hypertensive medication
Dyslipidemia	Total cholesterol equal or superior to 200 mg/dl and/or
LDL-cholesterol equal or superior to 115 mg/dl	
Smoking	Present or past smoker of at least 5 cigaretten daily
Obesity	Body mass index equal or superior to 30 kg/m ²
Abdominal obesity	Waist circumference equal or superior to 102 cm in males, respective 88 cm in females
Diabetes mellitus	Fasting glucose repeatedly equal or superior to 126 mg/dl and/or antidiabetic treatment

Materials and methods

This is a cross-sectional study, that included 130 consecutive patients with definite RA, according to the modified American Rheumatology Association criteria [8], admitted for active disease, in the Rheumatology Clinic, during a semester.

The patients were evaluated by the treating rheumatologist and by a cardiologist, using clinical examination, routine biochemistry, X-ray, electrocardiogram and cardiac ultrasound. For each patient we noted demographic data, the characteristics of the rheumatic disease, the presence of traditional c.v. risk factors (Table I) and the organic c.v. disease (Table II), if the case.

Table II. Organic cardiovascular disease

Cardiovascular disease	Description
Symptomatic coronary heart disease	Angina pectoris or Hystory of myocardial infarction
Symptomatic cerebrovascular disease	Stroke or Transient ischemic attack
Peripheral vascular disease	Symptomatic limb ischemia or Aortic aneurysm
Heart failure	Characteristic symptoms and signs and Cardiac dyfunction on cardiac ultrasound and/or Increased natriuretic peptides
Renal disease	Creatinin equal or superior to 1,5 mg/dl in males, respective 1,4 mg/dl in females or Proteinuria equal or superior to 300 mg/day

Patients were considered to be at high c.v. risk, if they had symptomatic c.v. disease, diabetes, or multiple risk factors, generating an estimated risk for fatal c.v. disease at 10 years of more than 5%. The risk for c.v. death at 10 years was estimated for such patients using the SCORE Table, that considers the age, sex, smoking status, hypertension and cholesterol level [9]. We used the SCORE variant for regions with high c.v. risk, as recommended for Romania. We finally introduced the correction suggested by EULAR [4], that is multiplying the risk by 1.5 - if RA fulfills at least two of the following features: long evolution of the disease, seropositivity and certain extraarticular involvement (Table III).

Table III. Rheumatoid arthritis characteristics that pose increased cardiovascular risk (Presence of at least two out of the three above features requires multiplication of SCORE risk by 1.5 (according to EULAR recommendation [4]))

Rheumatic disease evolution longer than 10 years
Seropositivity (rheumatoid factor and/or anti cyclic citrullinated peptide antibodies)
Extraarticular rheumatoid disease: rheumatoid nodules, vasculitis, pericarditis, Felty syndrome, neuropathy, rheumatoid lung, eye or renal disease

The preventive therapies checked for consistency with the guidelines [3,4,10] were antihypertensive medication, statins for dyslipidemia and antiaggregants in the patients with symptomatic atherosclerotic disease (Table IV includes also the goals for the first two therapeutic interventions). The results were compared with the observations from the general Romanian population (SEPHAR-Romania study [11]) and from the European population (EURIKA study [12]).

Statistical analysis was performed using SPSS 17.0. Continuous data were presented as mean, with standard deviation (SD) as the measure of spread; categorical data were presented as frequencies and percentages. Differences between categorical variables were searched using chi squared test.

Results and discussion

Demographic data and characteristics of RA

The mean age of the study group was 63.1 ± 10.2 years and 83% were women, features that are to be expected in a RA lot. The rheumatic disease was seropositive in 81.5% of the patients and extraarticular involvement was present in 70%. The mean Disease Activity Score (DAS28) was 5.02 ± 1.08 . These characteristics illustrate a group of hospitalized RA patients with a rather severe and active disease.

Prevalence of cardiovascular risk factors

The most frequent risk factors encountered were dyslipidemia (62.3%), hypertension (54.6%) and abdominal obesity (53%). The prevalence of the risk factors was generally similar to that reported in the SEPHAR-Romania study for the general Romanian population [11]. The only significant differences concerned the abdominal obesity – more frequent, and smoking – less frequent in the RA group (Figure 1). These differences are probably explained by the predominance of middle-aged women in the RA group.

Figure 1. Risk factors prevalence in rheumatoid arthritis (RA) lot, versus general adult Romanian population (Prevalence of risk factors in the general adult Romanian population is that reported in the SEPHAR-Romania study [11]; for hypertension we assumed the prevalence in persons older than 60 years, BMI = body mass index)

Organic heart disease and global cardiovascular risk

Organic heart disease was identified in 28.4% of the patients, and other 37.7% were at high c.v. risk based on an estimated risk of fatal cardiac disease at 10 years of more than 5%, according to the SCORE Table, with the correction for RA, as described above. Globally, 66.1% of the patients were classified as having high c.v. risk and thus had indication for intensive risk factors control. A substudy of SEPHAR-Romania identified 20.7% of the subjects among the general adult Romanian population as having a high c.v. risk [13], but no data are available concerning different age groups. Another Romanian study that involved four general practitioners from an urban area reported a prevalence of high c.v. risk of 39.2% among people older than 25 years of age [14].

Hypertension treatment and control

Hypertension was treated in 81.6% of the cases and controlled to the target values (lower than 140/90 mm Hg) in 70.4%. The percentages correspond to a significantly higher degree of treatment and control, versus both the general population of Romania (39% treated, 7% controlled) and the population older than 60 years (60% treated, 42% controlled) in the SEPHAR-Romania study [11] (Figure 2). For the situation of the general European population over fifty years of age, with at least one c.v. risk factor, EURIKA study reported a rate of 94% of hypertension treatment, but only a 37% rate of control to target values [12].

The high rate of hypertension treatment and control in our group of RA patients has probably more than one motivation: middle-aged women are more thoughtful about their disease and treatment; and these are patients with severe chronic rheumatic disease, who were repeatedly admitted to a reference tertiary care center, coming every few months in the attention of medical personnel, and by this having better opportunities to be diagnosed and treated for their comorbidities.

Figure 2. Hypertension treatment and control in rheumatoid arthritis (RA) lot, versus general Romanian and European population (Data concerning the Romanian population are from SEPHAR-Romania study and apply to population older than 60 years [11] Data concerning the European population are from EURIKA study [12] and apply to persons older than 50 years, with at least one coronary risk factor. Differences in the rates of hypertension treatment and control between the RA lot and the general Romanian and European population were statistically significant ($p < 0,05$))

Dyslipidemia treatment and control

Among the AR patients with dyslipidemia and indication for statin treatment, only 40.7% were treated and 22.2% were controlled to recommended target values. The rates are disappointingly low, either if we consider them as absolute frequencies, or in comparison with the rates reported in EURIKA study, for the European population (74% of dyslipidemia cases are treated and 30% are controlled to target values; only the difference in the rate of dyslipidemia treatment reached statistical significance) [12] (Figure 3).

The causes for dyslipidemia undertreatment in patients with active RA are partly similar to that in the general population: insufficient information about the guidelines recommendations, fear for adverse reaction, low compliance of the patients with a life-time treatment for an asymptomatic condition. Some other difficulties might be particular to RA patients: doctors and patients focus on the treatment of the painful and disabling rheumatic disease, and tend to neglect an apparently innocent biochemical

abnormality; concerns can arise about additive or confusing secondary effects (hepatotoxicity of statins and methotrexate, musculoskeletal pain induced by statin or in the context of the rheumatic disease). Although small to medium-sized studies demonstrated that statins are as useful [15] and safe [16] in c.v. prevention in RA patients, as they are in the general population, and that stopping statins can increase the incidence of acute myocardial infarction in RA patients [17], their use continues to be insufficient in this high risk subgroup [18]. The practicing physicians must bear in mind that statins represent the most effective drugs currently available for the reduction of low-density lipoprotein cholesterol, a critical therapeutic target for primary and secondary prevention of c.v. atherosclerotic disease.

Figure 3. Dyslipidemia treatment and control, in rheumatoid arthritis (RA) patients, versus European population (Data concerning the European population are from EURIKA study [12] and apply to persons older than 50 years, with at least one coronary risk factor)

Aspirin in the prevention of atherothrombotic events

Among the patients with symptomatic atherosclerotic disease, less than one half (48.6%) were treated with antiaggregants. European studies report a better antiaggregant treatment rate, but still a lower rate of aspirin use in the secondary prevention of atherosclerotic events in RA patients, comparative with the general population [18]. Although the indications for antiaggregant treatment are the same for the RA patients, as for the general population, adherence to the guidelines may be weaker in rheumatic patients because of the concern about the increased hemorrhagic risk when non-steroidal

anti-inflammatory drugs (NSAIDs) or steroids are co-administrated. This inconvenient can be actually mitigated by adding a proton pump inhibitor (PPI); fixed combinations containing a low dose of aspirin (or a NSAID) and a PPI are available, and can increase compliance, but these products are expensive relative to the individual generic products.

Conclusions

Cardiovascular risk factors were similar in the RA group with the general Romanian population, with the exception of abdominal obesity (more frequent) and smoking (less frequent). The most frequent encountered risk factors were dyslipidemia, hypertension and abdominal obesity.

Organic heart disease was identified in more than a quarter of the RA patients, and globally, one third of the total group had high cardiovascular risk, that imposes intensive risk factors control.

The rates of hypertension treatment and control were superior relative to the general Romanian population, but there still is space for improvement.

For dyslipidemia, the rates of treatment and control were low, and inferior to that of the Europeans older than fifty years.

Antiaggregants for symptomatic atherosclerotic disease were used in less than one half of the patients.

Both statins and aspirin were grossly underused in RA patients with high cardiovascular risk.

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