Epidemiology of rheumatoid arthritis: A literature review

Valbona Duraj, Argjent Tafaj, Teuta Backa

Service of Rheumatology, University Hospital Center "Mother Teresa", Tirana, Albania.

Corresponding author: Valbona Duraj, University Hospital Center "Mother Theresa";Address: Rr. "Dibres", No. 370, Tirana, Albania;
Telephone: +35567209363; E-mail: valbonaduraj@yahoo.com

Abstract

Rheumatoid arthritis is basically considered a clinical syndrome across several disease subsets characterized by systemic inflammation, persistent synovitis, and autoantibodies.
Genetic factors account for 50% of the risk of developing rheumatoid arthritis. In population-based studies in developed countries, it has been reported that rheumatoid arthritis affects 0.5%-1.0% of adults. The condition is three times more frequent in women than men. In both sexes, the prevalence increases with age. The prevalence of rheumatoid arthritis has remarkable geographical variations. The disease is more prevalent in Northern Europe and North America compared with many parts of the developing world. Nonetheless, valid and reliable data about developing countries and/or transitional societies are scarce.
The new classification criteria for rheumatoid arthritis, developed by the American College of Rheumatology and the European League Against Rheumatism, assess joint involvement, autoantibody status, and acute-phase response and symptom duration. Notwithstanding the unresolved difficulties and challenges related to management of rheumatoid arthritis, the ongoing introduction of ground-breaking treatments may turn out to be rather effective. In any case, it has been convincingly argued that the new direction of treatment and management of rheumatoid arthritis should be towards short intensive therapeutic courses that result in remission instead of the traditional approach that is long-term suppressive treatment strategies.

Keywords: arthritis, rheumatoid arthritis, rheumatic conditions, rheumatology.

Introduction

Rheumatoid arthritis is basically considered a clinical syndrome across several disease subsets (1), involving several inflammatory flows (2), leading to an ultimate common pathway in which persistent synovial inflammation and associated damage to articular cartilage and underlying bone are present (3). Classification criteria of rheumatoid arthritis

were developed about 50 years ago (4).

In the pathophysiology of the rheumatoid arthritis, a main inflammatory process includes overproduction of the tumor necrosis factor (3,5) which, in turn, leads to overproduction of many cytokines such as interleukin 6, which causes persistent inflammation and joint destruction (3,6).

Genetic factors account for 50% of the risk of developing rheumatoid arthritis (7,8) and are mainly associated with either autoantibody-positive disease (ACPA-positive) or ACPA-negative disease (3). ACPA-positive disease is associated with increased joint damage and low remission rates (9). Smoking, which is the most frequently studied environmental factor for rheumatoid arthritis (see below), appears to be a risk factor for ACPA-positive disease (10). In general, genetic research supports the idea that rheumatoid arthritis is a heterogeneous group of overlapping syndromes (3).

Diagnostic classification of rheumatoid arthritis

Early classification criteria for rheumatoid arthritis were designed to distinguish established rheumatoid arthritis from other types of established joint diseases (3,4). For this purpose, researchers and clinical epidemiologists conducted studies including homogeneous patients' groups; this was particularly the case in clinical trials (3).

The American College of Rheumatology criteria developed in 1987 (4) have demonstrated poor sensitivity and specificity for classification of patients with early inflammatory arthritis as having rheumatoid arthritis (11). These criteria have failed to identify individuals with very early arthritis who subsequently develop rheumatoid arthritis (12). Nowadays, effective treatment in early arthritis prevents or delays patients fulfilling the 1987 American College of Rheumatology criteria and, therefore, new classification criteria need to be endorsed.

Table 1 presents the new classification criteria for rheumatoid arthritis (3). These criteria were

Table 1. Classification criteria for rheumatoid arthritis – American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR), 2010

ACR/EULAR 2010 criteria (3,11)
1. *Joint involvement (0–5)* • One medium-to-large joint (0) • Two to ten medium-to-large joints (1) • One to three small joints (large joints not counted) (2) • Four to ten small joints (large joints not counted) (3) • More than ten joints (at least one small joint) (5) **2. *Serology (0–3)*** • Negative RF and negative ACPA (0) • Low positive RF or low positive ACPA (2) • High positive RF or high positive ACPA (3) **3. *Acute-phase reactants (0–1)*** • Normal CRP and normal ESR (0) • Abnormal CRP or abnormal ESR (1) **4. *Duration of symptoms (0–1)*** • Less than 6 weeks (0) • Six weeks or more (1)
Points are shown in parentheses. Cut-point for rheumatoid arthritis: ≥6 points. *Patients can also be classified as having rheumatoid arthritis if they have:* *a) typical erosions;* *b) long-standing disease previously satisfying the classification criteria.*

developed by the American College of Rheumatology and the European League Against Rheumatism to classify both early and established disease (13). These new classification criteria for arthritis assess joint involvement, autoantibody status, and acute-phase response and symptom duration (3,13). The effect on diagnosis and management of these new criteria will become clearer gradually over the next few years.

Frequency of rheumatoid arthritis

It must be noted that estimates of the frequency of rheumatoid arthritis vary depending on the methods used to determine its presence (3,14,15). In population-based studies in developed countries, it has been reported that rheumatoid arthritis affects 0.5%-1.0% of adults (3). The condition is three times more frequent in women than men (3). In both sexes, the prevalence increases with age. In women, the prevalence of rheumatoid arthritis is highest among those over 65 years, which suggests that hormonal factors could play a pathogenic role (16). Incidence of rheumatoid arthritis ranges from 5-50 per 100,000 adults in developed countries and increases with age (17). Data about developing/ transitional countries are scarce.

As for the prevalence of rheumatoid arthritis, it has remarkable geographical variations (18). The disease is more prevalent in Northern Europe and North America compared with many parts of the developing world and/or transitional countries, such as e.g. rural West Africa (19). It has been argued that these geographical variations maybe linked to different genetic predispositions, but are also related to different environmental factors which expose individuals from different regions in the world to different levels of risk for acquiring the disease (3).

Environmental risk factors of rheumatoid arthritis

Smoking is reported as the main environmental risk factor which increases twice the risk of developing rheumatoid arthritis (20). As mentioned earlier, the effect of smoking is restricted to patients with ACPA-positive disease (10). However, at a population level, the risk linked to smoking is too low to be clinically relevant notwithstanding the pathogenetic importance of this agent (3).

Other potential environmental risk factors for development of rheumatoid arthritis may include alcohol consumption, coffee intake, vitamin D status, and oral contraceptive use (3,21). Nevertheless, the evidence on the impact of these putative risk factors is controversial.

Clinical assessment of rheumatoid arthritis

The main assessment in rheumatoid arthritis pertains to joint inflammation (2), as presented in Table 2.

Table 2. Assessments in rheumatoid arthritis (source: Scott DL et al., 2010)

Assessments in rheumatoid arthritis (3)
Disease activity
Core assessments
• Joint counts (tender and swollen joint counts)
• Global assessment (doctor and patient) and pain score
• Laboratory (erythrocyte sedimentation rate and C-reactive protein)
• Disability (eg, health assessment questionnaire)
Additional assessment
• Fatigue
• Radiological damage
Combined status indices
• Disease activity score
• Simple disease activity score
• Clinical disease activity score
Change in status (trials only)
• ACR20, ACR50, and ACR70 responders

Assessments in rheumatoid arthritis (3)

Extra-articular disease

- Nodules
- Pulmonary
  - Pulmonary nodules
  - Pleural effusion
  - Fibrosing alveolitis
- Ocular
  - Keratoconjunctivitis sicca
  - Episcleritis
  - Scleritis
- Vasculitis
  - Nail fold
  - Systemic
- Cardiac
  - Pericarditis
  - Pericardial effusion
  - Valvular heart disease
  - Conduction defects
- Neurological
  - Nerve entrapment
  - Cervical myelopathy
  - Peripheral neuropathy
  - Mononeuritis multiplex
- Cutaneous
  - Palmar erythema
  - Pyoderma gangrenosum
  - Vasculitic rashes
  - Leg ulceration

Amyloidosis

Comorbidities

Cardiovascular

- Myocardial infarction
- Heart failure
- Stroke
- Peripheral vascular disease

Doctor-based reviews include overall estimates of disease activity and health status as evidenced by swollen and tender joint counts, as well as a global assessment of patient's conditions. Standard joint counts focus on 28 joints in the hands, upper limbs, and knees; joints in the feet are not included notwithstanding their clinical importance (3). Some experts prefer extended 66 and 68 joint counts including the feet. Laboratory parameters include erythrocyte sedimentation rate, C-reactive protein, or both (3).

Patient-based measures assess pain, global assessment, and disability (22), as determined through the health assessment questionnaire. Patients themselves document other relevant disease characteristics, such as fatigue and depression (3). It has been argued that patient-based measures are especially important to assess the individual's perspective of the burden of rheumatoid arthritis (3).

Management of rheumatoid arthritis

Currently, there exist several guidelines and protocols for management and treatment of rheumatoid arthritis which have been developed by the American College of Rheumatology, the European League Against Rheumatism and the UK's National Institute for Health and Clinical Excellence (3,23-25). Analgesics reduce pain, and non-steroidal anti-inflammatory drugs (NSAIDs) diminish pain and stiffness. Both groups of drugs are used widely to control symptoms of rheumatoid arthritis (3). NSAIDs have lost their traditional role as first-line treatment because of concerns about their limited effectiveness, inability to modify the long-term course of disease, and gastrointestinal and cardiac toxic effects (26).

Disease-modifying anti-rheumatic drugs (DMARDs) are used to reduce joint swelling and pain, decrease acute-phase markers, limit progressive

joint damage, and improve function (3). Methotrexate is the dominant DMARD. Sulfasalazine and leflunomide are also widely used effectively (3).

Biological agents are used when arthritis is uncontrolled or when DMARDs exhibit toxic effects (3). Tumor necrosis factor inhibitors were the first biological agents (3).

Nonetheless, the ultimate goal for management of rheumatoid arthritis would be a long-term remission induced by intensive, short-term treatment selected by biomarker profiles (3).

Conclusion

Currently, there are many unresolved difficulties for people suffering from rheumatoid arthritis. Nevertheless, the ongoing introduction of innovative and ground-breaking treatments can overcome many of these difficulties and challenges. One of the main requirements involves the characterization of disease subsets in individuals with early onset of rheumatoid arthritis in order to target intensive treatment regimens at patients who most need them and are likely to respond (3). From this point of view, it has been convincingly argued that the new direction of treatment and management of rheumatoid arthritis should be towards short intensive therapeutic courses that result in remission instead of the traditional approach that is long-term suppressive treatment strategies.

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