Diagnosis of Sjögren's Syndrome
American-European and the American College of Rheumatology Classification Criteria

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KEYWORDS

• Sjögren's syndrome • Diagnosis • Classification

KEY POINTS

- The terms diagnostic criteria and classification criteria for Sjögren's syndrome (SS) are frequently used interchangeably, although they represent different concepts; therefore, the differences are highlighted.
- Advances in the understanding of SS create the need for refinement of classification criteria.
- The major differences between and the strengths and weaknesses of the American European Consensus Group Criteria and the American College of Rheumatology (ACR) criteria for SS are addressed.
- Application of the more stringent ACR classification criteria in clinical practice may have an effect on reported prevalence of the disease.

INTRODUCTION

Sjögren's syndrome (SS) is a chronic, systemic autoimmune disorder with multiple organ system involvement, which lacks 1 single objective diagnostic gold standard, making diagnosis challenging. This situation is also true in other rheumatic diseases, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Each of these diseases has its own unique combination of clinical and laboratory manifestations, which are relied on when making a diagnosis. The clinician's judgment is the closest thing there is to a gold standard for diagnosis.

Classification criteria are used as a formalized approach to studying the course and management of rheumatic diseases and provide a conceptual base for measuring future improvements in clinical care. They usually focus on clinical objectives to improve clinical research activities.[1] They are dynamic and continually evolve, as our understanding of the disease increases. Diagnosis differs from classification criteria in that the latter attempts to categorize a more homogeneous population in an attempt to better assess response to treatments.

Since 1965, there have been 11 sets of classification criteria for SS.[2–12] Past classification criteria contain a combination of subjective and objective findings in 3 areas of specialty practice: rheumatology, ophthalmology, and oral medicine. Criteria

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sets generally include the presence of serologic markers, objective oral and ocular findings assessing either function or changes in gland architecture or degree of damage, and subjective oral and ocular complaints.

Criteria sets have assessed glandular changes by the presence of focal lymphocytic infiltration or focus score (FS). This pathologic process occurs within the lacrimal glands, all 4 of the major salivary glands as well as the labial minor salivary glands (LSGs). Biopsy of the labial minor salivary gland is a less invasive procedure compared with biopsy of one of the major salivary glands or the lacrimal glands and is therefore the procedure of choice. One limitation associated with the LSG biopsy is that the sensitivity and specificity of this test vary widely (63%–93% and 61%–100%, respectively).[13] To complicate matters, the prevalence of focal lymphocytic infiltration in postmortem LSG studies ranges from 0% to 22.4% in males and 0% to 35.7% in females.[14] In addition, recent studies have shown that there are significant discrepancies in the evaluation of LSG biopsies among different pathologists, different specialties, and different specialty centers.[15,16] For this reason, classification criteria sets varied in what was considered a positive FS, ranging from an FS of more than 1 to 1 or more. Other objective tests of salivary gland function include salivary flow rates, scintigraphy, and sialography. These tests are associated with a variety of limitations, which are covered in more detail later.

Autoantibodies are another common component of classification criterion. Anti-Ro/SSA and anti-La/SSB antibodies are among the most frequently detected autoantibodies against extractable nuclear antigens associated with SS. Problematically, SSA has also been associated with SLE, systemic sclerosis, polymyositis, primary biliary cirrhosis, dermatomyositis, mixed connective tissue disease (CTD), and RA. The pathologic role of these antibodies is still poorly understood. Higher titers of SSA and SSB are associated with greater incidence of extraglandular manifestations of SS such as purpura, leukopenia, and lymphopenia.[17] Other less specific markers of inflammation such as IgG, antinuclear antibody (ANA), erythrocyte sedimentation rate, and rheumatoid factor (RF) have been included in past criteria.

Several ocular tests have been proposed for use in the classification of SS. Tests include tear breakup time, Schirmer tests with and without anesthesia, clearance tests, corneal esthesiometry, corneal and conjunctival staining with differing scoring and staining methods, and imprint cytology. These tests assess the ability of the lacrimal glands to function, the integrity of the tear film layers, or damage or deficits of the ocular surface.

Most of the previous classification criteria sets also included the presence of subjective symptoms of oral and ocular dryness in addition to these objective measures. The most commonly used symptom assessment criteria involve a positive response to at least 1 of the following 3 questions related to ocular symptoms: “Have you had daily, persistent, troublesome dry eyes for more than 3 months?”; “Do you have a recurrent sensation of sand or gravel in the eyes?”; and “Do you use tear substitutes more than 3 times a day?” Assessment of oral symptoms involves a positive response to at least 1 of the following: “Have you had a daily feeling of dry mouth for more than 3 months?”; “Have you had recurrently or persistently swollen salivary glands as an adult?”; and “Do you frequently drink liquids to aid in swallowing dry food?” The problem with assessing subjective complaints when determining SS classification is that dry eye and dry mouth symptoms are common and nonspecific.

According to the Dry Eye Workshop 2007 report, prevalence of dry eye ranges from 5% to 30% in people aged 50 years and older.[18] The prevalence of dry eye syndrome in the United States is estimated to be 3.2 million women and 1.7 million men, for a total of 4.9 million patients 50 years and older.[19] Prevalence estimates of xerostomia fluctuate depending on the population being studied but have been reported as high as 24.8%.[20]

Classification criteria are intended to provide a formalized approach to studying course and management of rheumatic disease, as well as a measure of improvement in clinical care. Understanding the purposes of specific criteria sets and the differences between different criteria categories is crucial for understanding the rheumatic disease literature and for the design and conduct of clinical and epidemiologic investigations.[1] In this article, the similarities and differences between the American-European Consensus Group Criteria (AECG)[9] and the newly proposed American College of Rheumatology (ACR) classification criteria for SS are described.[21] The clinical implications of switching to the ACR classification criteria from the AECG are also explored.

AECG CRITERIA

The AECG criteria (**Box 1**) published in 2002 were developed after criticisms were raised about the European Study Group on Classification Criteria (ESGCC) for SS,[8] which were developed and validated between 1989 and 1996 and were subject to certain bias based on a combination of ocular