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Editorial

Which Criteria to use for the Diagnosis of Behcet's Disease: International Study Group (ISG) Criteria or International Criteria for Behcet's Disease (ICBD)?

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Editorial

It is interesting to note that Behcet's Disease (BD) is one of those diseases which had an early diagnostic criteria (9 years after its official recognition, with the Curth criteria in 1946), having one of the largest number of classification/diagnosis criteria (17 sets, in 70 years, till 2016), among them only 2 real International Criteria (ISG and ICBD), and having one of the largest international participation (27 countries for ICBD). The ISG criteria were created by the collaboration of 7 countries (France, Iran, Japan, Tunisia, Turkey, UK, and USA) in 1990 [1-2]. The ICBD was first presented in 2006 to the International Conference on Behcet's Disease in Portugal and the revised version in 2010 to the International Conference on Behcet's Disease in London, and published in 2014 [3].

The sensitivity of ISG criteria was very good, at 92%, when checked on the patients gathered from the 7 countries. The specificity was excellent at 97%. Originally, the accuracy was not checked and instead the relative value, which was 189 (the sum of sensitivity and specificity). When the performance of the criteria was checked, for validation, in different countries, the sensitivity was low, while the specificity was high [4-10]. The problem came from two main biases. First, as the majority of BD patients gathered from the seven countries had oral aphthosis (OA), this manifestation was put as a mandatory symptom to be present for diagnosis, while all over the world, when patients are diagnosed by expert opinion, around 5% of patients diagnosed as having BD miss OA. Second, the patients' selection: overall 886 BD patients and 97 control patients were selected from the seven collaborating countries, with 366 (41.3%) from Iran, 285 (32.2%) from Turkey, and 141 (16.9%) from Japan, which made 90.4% from 3 countries and less than 10% of the remaining 4 countries. From Western countries, only 5% had BD. To be classified as having BD, a patient must have oral aphthosis (mandatory), and two of he following manifestations: genital aphthosis, skin manifestations (pseudo-folliculitis, erythema nodosum), ophthalmologic manifestations (anterior uveitis, posterior uveitis, retinal vasculitis), positive pathergy test.

For ICBD, patients were gathered from 27 countries, all over the world. This time, it was paid enough attention to not make the same error in the patient selection, and to have enough patients from the Western world. A total of 2556 BD and 1163 controls were gathered, with 35.1% from 9 countries of the Western world. The revised ICBD performance in the cohort of the international patients was: sensitivity 96%, specificity 91.2%, and accuracy 94.5%. ICBD was validated in Germany, China, Iran, and Italy [11-14]. The revised ICBD was validated in Iran [15] with sensitivity 96.8% (ISG 78.1%), specificity 97.2% (ISG 98.8%), and accuracy 97% (ISG 85.5%). To be classified as having BD, a patient must get 4 points from the ICBD. Oral aphthosis, genital aphthosis, and ophthalmologic manifestations (anterior uveitis, posterior uveitis, retinal vasculitis) get each 2 points. Skin manifestations (paseudo-folliculitis, erythema nodosum, skin aphthosis), vascular manifestations, neurological manifestations, and positive pathergy test get each one point.

As this validation in Iran was done on all the patients of the registry, from more than 40 years ago, it was interesting to see what will become the performance of the ISG and ICBD on BD and control patients of the 21 century (patients from the year 2000 up to 2016). The calculation was done on 3294 BD and 2581 control patients. The performance of ICBD versus the ISGwas for sensitivity 97.4% vs 66.7% (difference 30.7%), specificity 97.5% vs 99.7% (difference 2.2%), and accuracy 97.4 vs 81.3% (difference 16.1%). Another figure of importance is the optimization, which is the difference between the sensitivity and the specificity. A good optimization shows that the criteria set has the same ability to recognize the disease from the non-disease cases [16]. Smaller the optimization, better is the performance. The optimization of the ISG is 33.3, while the ICBD is only 0.1. One of the major problems of ISG is its very high specificity against the very low sensitivity. The big problem of ISG, in research studies, is to not recognize a large proportion of patients with the disease, and not include them in the study. Therefore, it may arrive to conclusions that may be harmful to a group of patients.

In conclusion, ICBD is much more performing than the ISG, due to its high accuracy and its excellent optimization. It is well suited for both diagnosis and classification purposes.

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