Internationally-accepted diagnostic criteria for Complex Regional Pain Syndrome (CRPS) are published by the International Association for the Study of Pain (IASP; [13]). The Sumitani et al. study in this issue [15] sought to replicate, in Japanese CRPS patients, previous diagnostic validation work conducted in largely Caucasian CRPS samples. This prior work found that the IASP diagnostic criteria displayed poor specificity, potentially leading to overdiagnosis of CRPS [3,6,8]. In response, modified empirically-derived diagnostic criteria for CRPS (referred to as the “Bruehl Criteria” in the Sumitani et al. paper) were put forth in 1999 [3,8]. These criteria and decision rules were slightly modified at an international consensus meeting held in Budapest, Hungary in 2003. The resulting “Budapest Criteria” have been proposed as a replacement for current IASP criteria [7].

International collaborative research to validate further the Budapest criteria has been ongoing, but in a primarily non-Asian sample, as in the original validation studies. Sumitani et al. report the first systematic data on CRPS diagnostic characteristics in a large Asian sample. They suggest that optimal CRPS diagnostic criteria and decision rules may differ between Japanese and Western patients. The authors propose empirically-derived CRPS criteria, which loosely parallel the Budapest criteria but are optimized for the Japanese population.

The work by Sumitani et al. raises interesting questions. Why might studies using similar methodology in patients who all meet the same IASP criteria produce notably different patterns of CRPS characteristics in Asian versus non-Asian samples? More pragmatically, does CRPS actually differ so extensively across cultures that different diagnostic criteria are required for accurate diagnosis?

It may be useful first to consider the pathophysiological mechanisms underlying CRPS. Current research supports a likely contribution of central and peripheral sensitization, inflammation, alteration of sympathetic and catecholaminergic function, altered limb representation in the somatosensory cortex, genetic factors, and psychophysiological interactions (see [2] for a review). These mechanisms can lead to characteristic signs of CRPS, such as allodynia and hyperalgesia (central and peripheral sensitization); redness, edema, and sweating changes (proinflammatory cytokines and neuropeptides; [1]); and temperature asymmetry (altered sympathetic and catecholaminergic function). Given the absence of studies directly comparing CRPS in Asian versus Western patients, it is not clear whether physiologically-determined clinical signs of CRPS indeed differ cross-culturally. One argument against such differences, for example, is that proinflammatory cytokines should produce redness and edema in both Japanese and Western CRPS patients. However, genetic work indicates that certain human leukocyte antigen (HLA) alleles may increase CRPS risk [4,16] and relative frequencies of various HLA alleles differ across Caucasian and Asian populations [11]. The possibility of physiologically-determined differences in CRPS presentation between these populations therefore cannot be ruled out.

It may also be important to consider non-physiological factors. All patient-reported symptoms used in CRPS diagnosis are by definition subjective, and even supposedly objective diagnostic signs, such as allodynia, hyperalgesia, and range-of-motion impairments on clinical examination, rely on patient reports of pain and thus are at best only semi-objective. In some cases, racial and ethnic factors appear to alter pain responsiveness and symptom reporting [5,10,12,14]. Thus, any CRPS diagnostic characteristic that is not purely objective (e.g., quantitative temperature asymmetry) may be influenced by these racial/ethnic factors. This is one pathway by which systematic differences between cultures in patterns of diagnostic CRPS signs and symptoms might occur.

Do such influences account for any cultural specificity in CRPS expression? Occurrence rates for self-reported symptoms in Table 2 of the Sumitani et al. study are comparable to those in the Harden et al. study [8], with the exception of a 20% lower rate of self-reported hyperesthesia and an 18% higher rate of skin changes in the former. Objective clinical signs showed more substantial differences. For example, trophic changes to skin and nails were observed at a 20% and 16% higher rate respectively, sweating changes at a 12% higher rate, temperature asymmetry occurred at a 20% lower rate, and objective muscle weakness at a 25% higher rate in the Sumitani et al. study [15] compared to Harden et al. [8]. The finding that objective signs showed more differences between Japanese and Western CRPS patients than did subjective symptoms suggests that factors other than ethnocultural symptom reporting differences may need to be considered.

Sample differences can be anticipated between two methodologically similar diagnostic validation studies, due simply to random sampling variability. There may also be systematic differences across studies due to differing clinic referral patterns (predominance of severe, treatment-resistant CRPS referrals versus more acute, primary care referrals). Statistical analyses used in the Sumitani et al. and prior diagnostic validation studies may be influenced by the distribution of signs and symptoms in the particular sample. Moreover, it is important to recognize that accuracy of diagnostic decision rules will be inflated in the sample in which they were derived as compared to independent cross-validation samples. Diagnostic accuracy of decision rules reported in both the Sumitani et al. [15] and Bruehl et al. [3] studies likely represent overestimates of diagnostic accuracy on replication. Consistent
with this, our recent collaborative work to validate the Budapest criteria (detailed in this issue of Pain [9]) suggests modest shrinkage in diagnostic specificity on cross-validation.

Sumitani et al. raise the idea of region-specific diagnostic criteria for CRPS, although acknowledge potential drawbacks. It is this author’s opinion that having diagnostic criteria that vary by region is inadvisable unless there is compelling evidence in favor of such a radical change. There are obvious advantages to having a single set of internationally-accepted diagnostic criteria to facilitate clinical communication and research sample generalizability. In contrast, there are obvious disadvantages to multiple region-specific diagnostic criteria, particularly the risk that they might lead back to the “Wild West” of CRPS diagnosis existing prior to 1994. It is not yet known whether differences between the Sumitani et al. and past CRPS diagnostic validation studies reflect random sample variability, or rather, real racial or cultural differences in CRPS expression. Whichever is the case, the field would clearly benefit from large international collaborative studies with diverse national, racial, and ethnocultural representation to address pathophysiology, diagnosis, and treatment of CRPS.

Conflict of interest statement

The author has no conflicts of interest to report.

References


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