Conwell TD, Hobbins WB, Giordani J. Sensitivity, Specificity, and Predictive Value of Infrared Cold Water Autonomic Functional Stress Testing, As Compared With Modified IASP Criteria for CRPS. Thermology International 2010;20:2.

Reviewed, no change to conclusions, February 2017

Design: Consecutive case series

Population/sample size/setting:

- 143 consecutive patients (89 women, 54 men, age range 21-72) referred to an infrared imaging facility for evaluation of presumptive CRPS
- Most had unilateral extremity involvement, either upper (n=84) or lower (n=54); 5 patients had involvement in all 4 extremities and 5 had involvement of 3 extremities

Main outcome measures:

- Purpose of the study was to evaluate infrared imaging to diagnose CRPS
- Each patient had an initial clinical examination for CRPS using the modified IASP research diagnostic criteria: both symptoms and signs of sensory, vasomotor, sudomotor, and motor/trophic changes, with evidence of continued pain disproportionate to the inciting event, in the absence of other diagnoses that better explain the signs and symptoms
- After classification as positive or negative with the IASP criteria, each patient had an infrared imaging test of central autonomic function
- A baseline infrared image was taken after the patient sat in a room at 20° C for 15 minutes to equilibrate body temperature
- The imaging test required the patient to immerse an uninvolved extremity in cold water (16° C) for 5 minutes, after which a second infrared image was taken of the involved extremity
- If the autonomic nervous system is intact, the expected response of the involved extremity is vasoconstriction, manifested as a cooling of the involved extremity, with a grey infrared subtraction image
- If the autonomic nervous system is compromised, the expected response is axonal vasodilatation with warming of the involved extremity, with a color infrared subtraction image
- By IASP criteria, there were 39 positive CRPS cases and 104 negative cases
- The infrared test was positive for autonomic failure in 28 of the 39 positive IASP cases, for a sensitivity of 72%
- The infrared test was negative in 98 of the 104 negative IASP cases, for a specificity of 94%
- The positive predictive value of the cold water test was 82% and the negative predictive value was 90%
- The kappa statistic was 0.69, indicating substantial agreement between the diagnosis made by IASP criteria and the autonomic inhibition manifested by the cold water immersion test

Authors' conclusions:

- The thermoregulatory dysfunction of CRPS is characterized by central inhibition of autonomic cutaneous vasoconstriction
- This inhibition of sympathetic vasoconstriction is manifested by paradoxical vasodilatation and warming of the involved limb, which can be detected by thermal subtraction imaging
- Cold water autonomic functional stress testing can enhance the diagnostic validity of the IASP criteria and lead to improved clinical care of CRPS

Comments:

- The primary purpose of the study appears to be to advance scientific understanding of the pathophysiology of CRPS, especially that of central autonomic dysfunction
- The role of the cold water test in the diagnosis of CRPS is not clearly defined
- It is not clear whether the IASP diagnoses are the gold standard against which the cold water tests are measured for sensitivity and specificity; usually, the definition of sensitivity and specificity are made with reference to such a standard
- The spectrum of patients appears to be appropriate for evaluating the performance of a diagnostic test; it consists of patients who would usually receive the test in clinical practice, in whom there is a reasonable index of suspicion, but for whom the resolution of diagnostic uncertainty is needed
- The CRPS evaluations using IASP criteria were done as the patients entered the study, and the cold water tests were done later; it is not clear whether these were done by the same clinicians, or if the interpreters of the cold water test were unaware of the IASP diagnoses
- If the cold water test interpreters were not blinded to the IASP diagnoses, the potential for bias arises, and the usefulness of the test is uncertain
- The cold water test relies on thermal subtraction imaging, and, since the results are classified as dichotomous (positive or negative), there is presumably a threshold that cleanly divides them; it is not clear whether all observers would define the threshold in the same way
- This question would be clarified if there were a measure of inter-rater reliability (such as kappa), in which two test interpreters, working independently, agree at a level of 0.6 or more
- The kappa statistic as presented shows agreement between the IASP and cold water test, but generally diagnostic test performance (measured by sensitivity and specificity) is not evaluated with a kappa statistic, which measures agreement beyond that which is expected by chance
- The study may be interpreted as showing that central autonomic dysfunction occurs in most, but not all, patients who have CRPS by IASP criteria
- The suggestion that the response to the test may help to guide therapy is interesting, and deserves further elaboration; it may mean that interventions which target the sympathetic nervous system are appropriate in some patients and not in others

Assessment: For evidence that cold water thermography diagnoses CRPS: indaequate