Invited Commentary

Clinical Diagnosis—Is There Any Other Type?

Gurpreet Dhaliwal, MD

In this issue of *JAMA Internal Medicine*, van der Geest et al[1] present a systematic review and meta-analysis of the diagnostic accuracy of symptoms, signs, and laboratory tests for giant cell arteritis (GCA). Their comprehensive review of 68 studies with 14 037 patients provides updated guidance for clinicians who assess the probability that a patient has GCA. This estimation drives decisions about temporal artery biopsy and glucocorticoid administration that include considerations of timing and logistics, patient comorbidities, coordination with consultants, and adverse effects of treatment. Giant cell arteritis is a disease that has no reference or "gold" standard test, yet once affixed to the record, it can set off a complicated diagnostic and therapeutic cascade.

Related article

The phrase *clinical diagnosis* features prominently throughout the review, including the Methods section, where many of the studies used a clinical diagnosis as the benchmark for GCA classification. Using clinical diagnosis as a reference standard in a meta-analysis conducted to improve clinical diagnosis may seem circular. So too, I learned, is that phrase.

Clinical Diagnosis

Clinical diagnosis is ubiquitous in medical parlance. However, when you listen or read closely, you learn that no one uses this phrase in the same way. A basic definition is a verdict made by history and physical examination alone, for example, lateral epicondylitis or rosacea.[2] *Clinical diagnosis* is also used when a simple confirmatory test, such as urinalysis to support a urinary tract infection diagnosis, or a costly exclusionary test, such as a magnetic resonance image of the brain to confirm an impression of ocular migraine, plays a part.

The role of testing and technology becomes confusing when you hear that "cardiac tamponade is a clinical diagnosis." The expression seems to imply that you should diagnose it from vital signs, neck veins, and a pulsus paradoxus, yet once cardiac tamponade becomes a plausible diagnosis, more people are looking for an echocardiogram than a sphygmomanometer. Perhaps what is meant is that the exclusive reliance on examination or echocardiography is a setup for diagnostic error,[3] and the balance between the two is what makes the diagnosis *clinical*.

Sometimes clinicians invoke the absence of a gold standard test (typically laboratory, imaging, or pathologic) as grounds for a clinical diagnosis. However, pursuit of the definitive laboratory or pathologic diagnosis never eliminates downstream potential for a clinical diagnosis. When the results—whether polymerase chain reaction analysis for severe acute respiratory syndrome coronavirus 2 or temporal artery biopsy findings—do not agree with our suspicions, we often remain undeterred and state with a mixture of trepidation and conviction, "I'm making a clinical diagnosis."

The proclamation often arises with an understanding that there is no such thing as a gold standard test with 100% sensitivity and 100% specificity in medicine. Every diagnostic test has an error rate that leads to patient misclassification.[4] To reduce this error, clinicians triangulate with other data points before they affix a diagnostic label.

Full Circle

Among the criteria for study inclusion in this meta-analysis were studies in which "a TAB [temporal artery biopsy], imaging test, or clinical diagnosis was used as the reference standard for GCA."[1] The authors explain that "clinical diagnosis could be based on defined criteria or judgment of 1 or more physicians."[1] This begs the question: What factored into those criteria and judgments?

The compendium of study-specific definitions in eTable 5 in the Supplement provides the answer and marvelously demonstrates the heterogeneity of what qualifies as a clinical diagnosis for GCA, not just in this meta-analysis but also in real life. Among 30 studies, there are more than 30 definitions. Some investigators make a clinical diagnosis based on the American College of Rheumatology classification criteria for GCA. Some use temporal artery biopsy results in their clinical diagnosis. Some use imaging for their clinical diagnosis. Some use response to treatment. Most use a combination.

Seeing laboratory, imaging, and biopsy results as part of a clinical diagnosis was confusing. I eventually discerned that *clinical diagnosis* means any instance in which an amalgamation of data takes precedence over the binary result of any test, even when that result is part of the calculus.

Temporal artery biopsy results can be falsely negative owing to the segmental nature of arteritis and in cases of GCA without temporal artery involvement. This makes a triangulation approach compulsory in a disease such as GCA, for which all reference standards (clinician judgment, imaging, and biopsy) are imperfect. When there is no gold, clinicians engage in alchemy. That alchemy is the clinical diagnosis.

Updating the Script

Van der Geest et al[1] did not seek a combination of signs, symptoms, and laboratory tests that allow the clinician to forgo testing or to treat with impunity; in nearly every case, additional data from a temporal artery biopsy or imaging are required to diagnose or exclude GCA with a high degree of certainty.[5] Instead, the authors provided updated test characteristics for familiar data points, such as jaw claudication or visual changes, and suggest modifications to our long-standing illness scripts (mental models of a disease's characteristic signs and symptoms) of GCA, for example, elevating the utility of limb claudication and reducing the value of headache as a discriminat-

ing feature. These insights refine pretest probability determinations and guide difficult point-of-care decisions, such as committing a frail patient to a temporal artery biopsy or deciding whether to start corticosteroid treatment immediately or await test results.

Show Your Work

This meta-analysis of signs and symptoms incidentally provided an occasion to examine the phenomenon that inspired the work in the first place: *clinical diagnosis*. Clinical diagnosis is both an all-encompassing and noninformative phrase. It keeps company with other ambiguous expressions in diagnostic medicine instruction: "You must maintain a high index of suspicion" (a nonsensical phrase because there is no diagnosis that you can reach by maintaining a low index of suspicion); "It's a diagnosis of exclusion" (all diagnoses requires excluding competing hypotheses; that is how diagnosis works); or "X is Y until proven otherwise" (which is almost existential, because anything could be something until proven otherwise).[6]

Teachers must do better than saying "it is a clinical diagnosis." They must instead articulate the specific elements that factor into a diagnostic label. Diagnostic criteria are codified in research studies, reference materials, and guidelines. However, in practice, the thresholds for the criterion data elements (cough, fever, infiltrate) are imprecise, and their utilities are perceived differently among clinicians (despite published test characteristics). I owe it to a learner, reader, or colleague to clarify that I diagnosed pneumonia based on A plus B plus C, fully acknowledging that you use A plus B plus D and find C (eg, crackles) less diagnostic than I do. This is laborious, and sometimes maddening, but refreshingly honest and straightforward.

Every diagnosis is an argument that is carefully constructed by the clinician. The data we use are never perfect, and neither are we. In that sense, every diagnosis is a clinical one.

ARTICLE INFORMATION

Author Affiliations: Department of Medicine, University of California, San Francisco; Medical Service, San Francisco Veterans Affairs Medical Center.

Corresponding Author: Gurpreet Dhaliwal, MD, Medical Service, San Francisco Veterans Affairs Medical Center, 4150 Clement St, San Francisco, CA 94121 (gurpreet.dhaliwal@ucsf.edu).

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