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An investigation into method of diagnosis in clinicopathologic conferences (CPCs)

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Abstract: An analysis of 50 clinicopathologic conferences (CPCs) reveals the method of diagnosis in them to consist of construction of exhaustive differential diagnosis followed by evaluation of each disease in it by the likelihood inference approach. This method leads to 98% diagnostic accuracy in these CPCs. A probabilistic approach is found not to be employed for evaluation of a disease.

Keywords: clinicopathologic conferences (CPCs); diagnosis; differential diagnosis; likelihood inference approach.

Introduction

Diagnosis is undoubtedly the most important step in taking care of a patient as the other two steps in patient care, treatment and prognosis, depend upon it. In general, a disease is diagnosed from evidence for it in a given patient, but what counts as evidence in actual practice is not always clear. In this paper, I examine 50 clinicopathologic conferences (CPCs) published in the New England Journal of Medicine to learn about the method of diagnosis employed by experienced physicians in real patients. This may help us understand and improve diagnosis in daily practice.

Methods

In each CPC, a clinician was provided with data consisting of observed facts about a real patient usually days or weeks before the public discussion of the case. In general, the data included symptoms, signs, routine laboratory and imaging test results, response to treatment given and the course of the patient’s illness.

In the publicly presented CPC, the clinician analyzed all this information and arrived at the most likely diagnosis which was confirmed or not to be correct by the presiding pathologist.

I examined 50 consecutive CPCs published from June 27, 2013 to October 15, 2015 in which the clinician did not know the diagnosis beforehand. I excluded CPCs published between these dates in which the clinician knew the diagnosis beforehand and those which were primarily about management, for example, of victims of the Boston Marathon bombing [1].

Results

In every CPC, the clinician analyzed and discussed the diagnosis in a given patient in four progressive stages as follows:

Stage I

In this stage, he or she selected a few key items which needed to be explained from the large mass of data provided. These items included symptoms such as rapid loss of vision [2], signs such as chest wall mass [3], bedside tests results such as ST elevation EKG changes [4], imaging study results such as discitis on an MRI of the thoracic spine [5], a syndrome such as presumed bacterial meningitis [6] and the temporal progression of an illness [7]. Only one item was identified in some patients [3] and multiple items in other patients [8] were identified.

Stage II

In this stage, items identified in Stage 1 were employed as clues to suspect a number of diseases which could possibly be present in the given patient. These suspected diseases formed an exhaustive differential diagnosis.

Stage III

In this stage, the merit of each disease in the differential diagnosis was evaluated with regard to its presence in the given patient.

Stage IV

In this stage, the disease with the greatest merit for being present was put forth as the most likely diagnosis. The
phrase ‘most likely’ was used for this one disease in 23 out of 50 CPCs and the phrase ‘most consistent with the patient findings’ was employed in six out of 50 CPCs. Other phrases employed for this disease in other CPCs included ‘disease fits almost all aspects of patient’s illness’ [8], ‘disease is best unifying diagnosis’ [9], and ‘this disease explains all key features of this patient’s presentation’ [10].

It should be noted the phrase ‘most probable’ was not employed to describe this one disease in any CPC.

In 36 out of 50 CPCs, the clinician mentioned the test which could confirm his or her most likely diagnosis.

In 49 out of 50 CPCs, the clinician’s most likely diagnosis was confirmed to be correct by a definitive test result presented by the pathologist.

Discussion

The 98% diagnostic accuracy achieved in these 50 CPCs is truly remarkable especially in view of the exceedingly complex and diverse presentations of the diseases discussed in them. Let us closely examine the diagnostic method employed which led to this near perfect accuracy.

The first important step taken by each clinician, I suggest, was to reduce the large mass of data provided to manageable proportions by selecting out a few key items that needed to be explained. With these items as clues, the clinician then suspected a number of diseases to form an exhaustive differential diagnosis. This was crucially important as the final correct diagnosis was included in differential diagnosis in 49 out of 50 CPCs. In the CPC with incorrect diagnosis, the correct diagnosis was not included in differential diagnosis.

As the status of all diseases in the differential diagnosis was merely that of hypotheses or possibilities, the next important step taken was to evaluate each of them for its presence in the given patient. This evaluation was performed in terms of a disease’s ability to explain key findings in the patient. If it failed to explain certain key findings, it was ruled out and if it explained most or all important findings, it was considered highly likely. This evaluation, performed in all CPCs, is illustrated by the following CPC [11], in which ‘common causes of abdominal pain – appendicitis, diverticulitis, cholecystitis, pancreatitis and renal colic as well as inflammatory bowel disease can be ruled out by the imaging and laboratory studies in this case’. In the same CPC, ‘i believe the most likely diagnosis in this case is lead poisoning which explains all the clinical, laboratory and imaging features including abdominal pain (lead colic), nausea, dysgeusia, constipation, pseudo-obstruction, joint and muscle pain, behavioral and cognitive changes, acute anemia, basophilic stippling, SIADH and decline in the blood level of phosphorus’.

The one disease out of all the other possible diseases in the differential diagnosis which best explained key features was put forth, as we note above, as the most likely diagnosis in a given patient.

We note that prior probability of a disease was not estimated and therefore the notion of prior evidence did not play any role in evaluation in any CPC. The presence of a disease was evaluated purely from findings in the patient that were provided. This together with the fact that the phrase ‘most probable’ was not employed to describe the best explanatory disease in any CPC clearly indicates, I suggest, that a probabilistic approach was not employed for evaluation.

The method of evaluation of a disease employed in these CPCs is best characterized as being Fisher’s likelihood inference method [12]. In this method, the likelihood of a hypothesis is proportional to probability of observed facts, given the hypothesis. In applying this method to evaluation, we consider all diseases in differential diagnosis as potential generators of findings (observed facts) in a given patient. The degree to which a disease is likely to be present (its likelihood) depends in this method upon the chance (probability) of findings being generated if the disease were actually present in this patient.

In brief, a clinician did not reason about how well the findings explained a disease, that is, he did not estimate probability of a disease given the findings. Instead, he reasoned about how well a disease explained the findings, that is, he estimated probability of the findings, given a disease. The former approach is probabilistic while the latter is likelihood based.

The effectiveness of the likelihood approach used in these CPCs is beyond doubt as it led to 98% diagnostic accuracy in them. A major reason for its effectiveness, I suggest, is that prior probability as prior evidence did not play any role in it. This allowed the presence of diseases with varying prior probabilities including those with low prior probabilities to be evaluated and thus diagnosed correctly. Thus diseases such as Pneumocystis pneumonia with HIV infection in absence of history of risk factors [13] and Wilson’s disease in the absence of neurologic abnormalities or psychiatric illnesses [14] were evaluated and diagnosed correctly despite their low prior probabilities, I suggest, due to employment of the likelihood inference method for evaluation.

The likelihood inference approach is essentially a method of comparative evaluation which allows us ‘to compare on some scale the merits of rival simple
hypotheses’ [15]. With it, ‘we choose the system which gives the highest chance to the facts we have observed’ [16]. This approach is ideally suited for diagnosis, as we saw in these CPCs, as we basically compare merits of different diseases in differential diagnosis given findings during diagnosis.

The likelihood of a disease needs to be carefully distinguished from the probability of a disease for which it is often mistaken. A likelihood, as pointed out earlier, has nothing to do with prior probability, while a (posterior) probability is generated from it. Furthermore, the likelihoods of different diseases, unlike probabilities of different diseases, in a given patient do not add up to 1 [15].

The present investigation is the first study, to the best of my knowledge, which examines the method of diagnosis in real patients. This method is found to consist of construction of an exhaustive differential diagnosis followed by evaluation of each disease in it by likelihood inference approach. This method leads to near perfect diagnostic accuracy in these CPCs.

This investigation also reveals, conclusively I believe, that a probabilistic approach was not employed for diagnosis in these CPCs. I could not find any other published study about diagnostic accuracy of a probabilistic approach in real patients in CPCs, clinical problem solving exercises, experimental studies or in daily practice. The prescription of this approach for diagnosis in daily practice [17] is thus similar to recommendation of a treatment whose efficacy has not been proven by clinical trials in real patients.

This study underscores the importance of differential diagnosis in diagnosis and thus strongly supports routine differential diagnosis in daily practice, which would be facilitated by a differential diagnosis generator such as Isabel [18]. Isabel included the correct diagnosis in differential diagnosis generated by it in 48 out of 50 cases in CPCs in a study about its accuracy [19].

In addition, it calls into question the value of a probabilistic approach which has been prescribed for diagnosis. Based on this study, adoption of a likelihood based approach for diagnosis in daily practice is likely to improve diagnostic accuracy in daily practice as well.

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