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Laboratory test interpretations and algorithms in utilization management

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ABSTRACT

Appropriate assimilation of laboratory test results into patient care is enhanced when pathologist interpretations of the laboratory tests are provided for clinicians, and when reflex algorithm testing is utilized. Benefits of algorithms and interpretations include avoidance of misdiagnoses, reducing the number of laboratory tests needed, reducing the number of procedures, transfusions and admissions, shortening the amount of time needed to reach a diagnosis, reducing errors in test ordering, and providing additional information about how the laboratory results might affect other aspects of a patient's care. Providing interpretations can be challenging for pathologists, therefore mechanisms to facilitate the successful implementation of an interpretation service are described. These include algorithm-based testing and interpretation, optimizing laboratory requisitions and/or order–entry systems, proficiency testing programs that assess interpretations and provide constructive feedback, utilization of a collection of interpretive sentences or paragraphs that can be building blocks ("coded comments") for constructing preliminary interpretations, middleware, and pathology resident participation and education. In conclusion, the combination of algorithms and interpretations for laboratory testing has multiple benefits for the medical care for the patient.

1. Introduction

Maintaining sufficient medical knowledge to manage patients is increasingly difficult for clinicians, as diagnostic and therapeutic options as well as laboratory test menus continue to expand. In addition, clinicians and pathologists are increasingly expected to provide care in a cost-effective and expedient manner, limiting unnecessary use of medical resources. Pathologists, as directors of clinical laboratories, can facilitate assimilation of the laboratory data into medically-appropriate and fiscally-efficient patient care by providing interpretations of laboratory data for the patient's medical record. Given the growing complexity of medical care, providing accurate interpretations can be a challenge for many pathologists. Algorithms and other approaches described herein augment a pathologist's ability to generate accurate interpretations.

2. The benefits of laboratory interpretations

Laboratory results substantially influence patient care. While laboratory testing represents only 3–5% of a hospital's budget, it impacts 60–70% of major medical decisions such as admissions, discharges, and medications [1,2]. In one study, only 61.7% received appropriate laboratory tests or radiography among 6721 adults, suggesting that clinicians need guidance in laboratory test utilization [3]. A cost analysis found that the coagulation laboratory interpretation service at our hospital could be saving our hospital one million dollars annually [2].

Interpretations of laboratory tests, provided by a laboratory pathologist or other qualified expert, can be very valuable for clinicians. Without an accompanying interpretation, laboratory tests can often be misinterpreted. For example, we encountered a patient who had been misdiagnosed with protein S deficiency during pregnancy, which had led her to abort her pregnancy because neither she nor her physician realized that protein S typically decreases during normal pregnancy, and she was afraid of developing recurrent venous thromboembolism. In another case, the diagnosis of von Willebrand disease was missed in a newborn, because the clinicians did not know that the diagnosis can be masked in neonates in that von Willebrand factor is typically elevated above a patient's baseline at birth. In addition, the newborn was ill from infection and internal bleeding at the time of testing, and acute illness also elevates von Willebrand factor above a patient's baseline. The missed diagnosis led to the baby's father being charged with child abuse for her bleeding episodes, and he was imprisoned. These two cases occurred at hospitals outside of our network where pathologists do not provide interpretations. In a third case, an experienced hematologist thought that slightly elevated hemoglobin A2 in a patient with sickle cell trait indicated co-existing beta thalassemia. Fortunately, this third case example occurred at our institution, which has been providing interpretations by pathologists for hemoglobin electrophoresis and other complex laboratory tests for the past 20 years. The interpretation for this patient stated that the results are consistent with sickle cell trait and concomitant alpha thalassemia trait, based on the relatively low

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percentage of hemoglobin S and the low MCV. Hemoglobin S can falsely elevate hemoglobin A2 due to co-elution, without beta thalassemia. Thus, a misdiagnosis was avoided.

At Massachusetts General Hospital, surveys of physicians receiving pathologist interpretations with their specialized coagulation test results showed that 98% find the interpretations "useful or informative." In addition, responses indicated that 72% of interpretations reduced the number of tests needed to make a diagnosis, 72% helped avoid a misdiagnosis, and 59% shortened the time to diagnosis [4]. In a subsequent, larger survey, also at Massachusetts General Hospital, 77% of responding clinicians indicated that the interpretations saved them time and 78% indicated that the interpretations impacted their differential diagnosis. Responses also indicated that overall the interpretations reduced the number of admissions, the number of procedures and laboratory tests performed, and the number blood products used [4]. More recently, a similar coagulation interpretation service was initiated at Cleveland Clinic, and a survey among clinicians using this service found similar results: the majority of respondents reported that the interpretations impacted the differential diagnosis, shortened the time to diagnosis, prevented misdiagnosis, reduced the number of laboratory tests performed, reduced the number of procedures performed, and led to a change in medications or blood product usage. A minority of respondents indicated that the interpretations avoided a hospital admission or reduced length of hospital stay [5].

Interpretations can also improve physicians' abilities to select the appropriate test(s) needed to reach or exclude a diagnosis. Laboratory test ordering patterns were studied immediately after we implemented a coagulation interpretation service for a group of outside hospitals, and the results were compared to ordering patterns after the interpretation service had been in place for 2.5 years. The number of coagulation test ordering errors decreased by nearly 2 errors per requisition during the study period ($P < 0.05$) [4]. Furthermore, initially, over 63% of requisitions had 4 errors, but at the end of the study period, this was reduced to only 10%. For example, clinicians had frequently ordered antigen assays (immunoassays) to assess for protein C, protein S or antithrombin deficiency, but after receiving interpretations for 2.5 years, they more frequently ordered functional assays, which are the appropriate tests to order. The interpretations include that antigen assays are inadequate because they are not able to detect type II (qualitative) deficiencies, as they do not assess protein function. In contrast, functional assays are able to detect both type I (quantitative) and type II deficiencies. The results of this study provided evidence that interpretations can successfully modify physicians' ability to order tests appropriately.

The value of the interpretations is maximized if all the relevant results for a specimen are interpreted together, while also taking into account the patient's medical history. That is to say, patient-specific interpretations are more valuable than generic interpretations. For example, if a patient has low protein C, low protein S, and normal antithrombin, it is most useful for the interpretation to indicate that the most likely explanation for this combination of findings is warfarin or vitamin K deficiency, rather than list all the possible causes of low protein C, and then separately list all the possible causes of low protein S. Incorporating the normal antithrombin result into the interpretation allows the exclusion of some other possible causes of low protein C and low protein S, or at least rendering them much less likely. The interpretation can also give suggestions for follow-up testing, if appropriate. In the current example, the interpretation would indicate that testing can be repeated any time when the patient has not had warfarin for at least 20 days, because it can take that long for protein S to recover to normal after warfarin discontinuation (protein C recovers more quickly, usually within 10 days).

In an additional example of the utility of including information from the patient's medical record to customize the interpretation, for a patient with low antithrombin and 3+ proteinuria on a urinalysis, the interpretation can note that proteinuria can cause an acquired loss of antithrombin. Other possible causes of low antithrombin can also be included for completeness.

Interpretations can also be an opportunity for the pathologist to comment on ways that the laboratory findings might significantly impact other aspects of the patient's care. For example, if a patient on warfarin tests positive for a lupus anticoagulant, the interpretation can notify clinicians that lupus anticoagulants are capable of artifactually prolonging the prothrombin time and international normalized ratio (PT/INR), potentially overestimating the patient's level of warfarin anticoagulation. The interpretation can note that a chromogenic factor X assay can be performed on this specimen if requested, to help determine whether or not the lupus anticoagulant is artifactually prolonging the PT/INR [6].

3. Challenges for the pathologist

The fund of knowledge required to care for patients is rapidly expanding not only for clinicians, but also for pathologists. This can be a barrier to the successful implementation of a laboratory interpretation service. For example, a survey of 81 specialized coagulation laboratories in the United States and Canada (38% responded) found inconsistent approaches to interpreting von Willebrand test results [7]. Five components, deemed important to include in an adequate interpretation, were appropriately addressed in interpretations performed by the following percentage of laboratories: von Willebrand factor increases with age (13%), pre-analytical variables can cause falsely low levels (38%), low levels can be congenital or acquired (58%), low levels should be confirmed by repeat testing (54%), blood type O individuals have lower levels (63%), and low levels can be due to other factors (e.g., illness, injury, pregnancy, stress, estrogen use (63%)). Thus, many laboratories do not include one or more of these elements in their interpretations, leaving room for improvement among North American laboratories. In addition, the cut-off used to define normal was variable [7].

In another study, pathologists and laboratory scientists in Asia and Africa were asked to interpret a series of laboratory results representing common problems encountered in clinical chemistry. The response rate was 50%. The authors reported variable quality of interpretations, with some providing incorrect or misleading information [8].

4. Mechanisms to facilitate successful interpretations

Given the difficulties for pathologists in providing interpretations as well as the challenges for clinicians in ordering the correct tests, the following section describes mechanisms that increase the likelihood of success for an interpretation service. These approaches include algorithm-based testing and interpretation, optimizing laboratory requisitions and/or order–entry systems, proficiency testing programs that assess interpretations and provide constructive feedback, the development of "coded comments", and pathology resident participation and education.

4.1. Algorithms and laboratory test requisitions

An interpretation service is more efficient when combined with strategic testing algorithms that simplify the diagnostic process for clinicians. Reflex test algorithms provide a faster route to reach a diagnosis and at lower cost, by avoiding unnecessary tests and blood sample collections [9]. Over 100 reflex testing algorithms are in use at our hospital, which have been approved by our hospital's medical policy committee [9]. Example test algorithms are shown in Fig. 1 (protein C) and Fig. 2 (celiac disease) [10,11]. Note that the algorithm for protein C testing incorporates information that is also useful for providing an interpretation, such as the various acquired conditions that can cause low protein C, the falsely normal results that can occur if patients are receiving novel anticoagulants that recently emerged on the market, and how long to wait after warfarin discontinuation before testing. A similar algorithm has also been published for antithrombin testing [12]. Note that the algorithm for celiac disease is also beneficial in controlling costs for send-out testing, by