Clinical Chemistry

Diagnostic Accuracy of Point-of-Care Fecal Calprotectin and Immunochemical Occult Blood Tests for Diagnosis of Organic Bowel Disease in Primary Care: The Cost-Effectiveness of a Decision Rule for Abdominal Complaints in Primary Care Study (CEDAR) Study

Bob Barrett: This is the podcast from *'Clinical Chemistry'*. I'm Bob Barrett. Abdominal pain, rectal bleeding, or altered defecation pattern are often presented by patients to primary care practitioners but finding out of these symptoms or a sign of organic bowel disease is not simple.

The prevalence of organic bowel disease including inflammatory bowel disease and colorectal cancer in primary care patients is relatively low. But the diagnostic workup aims at not missing organic bowel disease patients who require subsequent work-up and referral to secondary care.

Consequently, many patients are referred for secondary care endoscopy to rule out organic bowel disease. Endoscopy is a valuable procedure for diagnosing organic bowel disease, but is costly and carries risks, including bleeding and bowel perforation, and careful patient selection is important. Therefore, point-of-care test to determine whether a patient requires further examination can be extremely useful.

In the June 2012 issue of *'Clinical Chemistry,'* Dr. Liselotte Kok and colleagues from the University Medical Center, Utrecht in the Netherlands tested the available point-of-care tests for effectiveness and came to some startling conclusions. Dr. Kok is our guest in this podcast. Doctor why is this study important?

Dr. Liselotte Kok: Well, we think this study is important because it evaluates diagnostic test that may help the primary care physician discriminate better between patients with organic bowel disease, such as inflammatory bowel disease and colorectal cancer, and on the other hand, patients with benign bowel conditions. Patients with abdominal pain, rectal bleeding or change in bowel habit consult their primary care physician very frequently.

Diagnosis of organic bowel disease is challenging and the symptoms also features are more common benign conditions, such as irritable bowel syndrome.

Diagnostic criteria in several blood test evaluated for this purpose have been proven to lack specificity. As a result many patients are referred for colonoscopy as it is considered the gold standard for suspected organic bowel disease.

However, this is an uncomfortable procedure, has a low rate of important complications and scarce and costly. Thus simple, non-invasive test to better discriminate organic bowel disease from benign viral conditions are needed. Within the CEDAR study we evaluated three eligible fecal

tests, Calprotectin ELISA, Calprotectin Point-of-Care Test, and a Point-of-Care Fecal Immunochemical Test for hemoglobin.

Bob Barrett: Can you tell us something about the calprotectin and fecal immunochemical test?

Dr. Liselotte Kok: Yes of course. Fecal calprotectin, is a degradation product from neutrophil granulocytes from the mucosal layer of the colon, and is increased when colonic inflammation is present. Fecal calprotectin has been shown to have high diagnostic accuracy for discriminating organic bowel disease from benign bowel conditions in secondary care, but its value in primary care is not investigated yet.

And on the other hand, Fecal Immunochemical Tests detect hemoglobin and its early degradation products, which may indicate the presence of polyp or adenocarcinoma of the colon. This test have been extensively studied for screening on the colorectal cancer purposes in decent traumatic individuals, but evidence of the accuracy of this test in symptomatic individuals is harsh and lacking from primary care.

We used two point-of-care tests, that they have advantages for primary care. They are relatively inexpensive, are easy to perform and usually have a built-in positive control.

Bob Barrett: Now what were the main findings of the CEDAR study?

Dr. Liselotte Kok: We found that the diagnostic accuracy of the test alone or in combination was low, and all adenomas, irrespective of size were considered serious colorectal disease, but the smaller adenomas were classified non-organic bowel disease, the results improved.

Negative predictive values, a major determinant of clinical utility in this primary care setting, were above 90% for all tests Thus, that's why we were able to rule out organic bowel disease to a reasonable extent, nit only for each test taken individually, but even more so, when the blue print of characters were combined. This is very promising, because these tests could be used to reduce referrals for colonoscopy.

However, because negative predicted values were not 100%, Organic Bowel Disease patients will be missed and further more the test were not useful for ruling in, largely because calprotectin is a general closing marker of cut damage, so many patients incorrectly had high calprotectin concentrations.

Bob Barrett: How could this approach be improved so that serious colorectal disease will not be missed?

Dr. Liselotte Kok: Well it's very important to detect most colorectal disease and ideally never to miss colorectal neoplasia and other serious disease. We have evaluated the diagnostic accuracy of the test now in isolation, so without incorporating symptoms and signs of the patients, our next step would be to combine the test to the diagnostic algorithms based on symptoms and signs, and to see if negative predicted values can be improved.

Also, we have used the cutoff concentrations recommended by the manufactures of the test, but these might not be the optimal cutoffs.

It has been shown like calprotectin and hemoglobin concentrations may vary among certain subgroup so there might be a need to define optimal cutoff concentrations for patient group.

Bob Barrett: How do you think these results will impact clinical practice?

Dr. Liselotte Kok: If our approach can be approved so that serious colorectal disease will not be missed, we hope that primary care physicians will be able to use a new strategy in the near future.

If a patient presents with non-acute lower abdominal symptoms, and there is diagnostic uncertainty, a new strategy could be used to rule out organic bowel disease, and to reduce the number of unnecessary referrals to secondary care. This approach may yield a number of positive effects for individual patients and the health care system. The diagnosis and treatment of organic bowel disease can improve survival. The reduction of the rating list for colonoscopy and a reduction in healthcare cost and patients without serious colorectal disease, they will not need to undergo an invasive procedure as colonoscopy anymore.

Bob Barrett: Well finally doctor let's look ahead, give us an idea of where your future research will be going?

Dr. Liselotte Kok: Well, we are currently working on new results from the CEDAR study. We hope to develop a strategy that can rule out organic bowel disease safely by incorporating the calprotectin and fecal immunochemical test for hemoglobin and a scoring systems for organic bowel disease. Our aim is to develop and validate these scoring systems and to evaluate such an approach that's cost effective.

Bob Barrett: Dr. Liselotte Kok is University Medical Center, Utrecht in the Netherlands and has been our guest in this podcast from *'Clinical Chemistry'*.

I'm Bob Barrett. Thanks for listening!

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