Editorial Commentary

Inflammatory biomarkers and clinical judgment in the emergency diagnosis of urgent abdominal pain

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I reviewed with interest the paper by Breidthardt *et al.*, which reports the results of a study on patients presented to the emergency department with acute abdominal pain, who was investigated using the inflammatory markers interlukein-6 and procalcitonin to triage the urgency of the situation in conjunction with clinical judgment. The study is well designed and a few centers have participated with their patients.

Interleuki-6 had been studied in the past for right iliac fossa pain and other types of abdominal pain that ended up having non-conclusive results (1); and proved to be a useful tool to assess the severity of acute pancreatitis (2).

Most cases of abdominal pain are a mild self-limiting episode with no specific cause identified. It would be an achievement to come up with a readily available blood test (albeit combined with clinical suspicion) that can rule out those who have a self-limiting condition who can be reassured and discharged to avoid further investigations and the cost associated with hospital admission and unnecessary workup.

The clinical judgment of the urgency was assessed by the visual analog scale and those who scored 3–7 were considered as to have uncertain urgency or cause. Urea under the curve was constructed to determine sensitivity and specificity of the raised inflammatory markers and the clinical judgment and when the two were combined. The uncertainty of the diagnosis even after abdominal imaging was 49%; the requirement of imaging was very high in those who were considered uncertain according to the VAS of uncertainty 3–7.

The results showed the area under the curve (AUC) for elevated interleukin-6 (median 23 ng/L) for urgent pain was 0.8 compared with 0.65 for calcitonin and 0.69 for clinical judgment (P<0.0001). Integrated decision improvement analyses showed that interleukin-6 resulted in net improvement in mean predicted probability by +16% (P<0.0001). These results showed that interleukin-6 have performed better than WBC and CRP. The combination of clinical judgment and interleukin-6 at presentation resulted in AUC of 0.83, which significantly improved the diagnostic accuracy over the initial clinical assessment. The increased diagnostic yield of adding interleukin-6 was assessed using reclassification tables for net reclassification improvement (NRI) that showed an improvement by 27.3%. In that classification; in the non-urgent group 111 patients (16.7%) moved correctly downward (certainly non-urgent, or became true negative) and 23 patients (3.5%) moved incorrectly upward in the classification (became false positive).

In the urgent group 85 patients (22.6%) correctly moved upward (became true positive), and 32 patients (8.5%) incorrectly moved downward (became false negative). There was improvement in integrated discrimination of median predicted probability by +19% compared with clinical judgment; authors did not mention the negative counterpart of that but I assume it is 27.3% and the 19%.

Interleukin-6 was retested 3hrs after the initial sample that was taken at arrival; those with levels <2.4 ng/L ruled out as non-urgent with 97% sensitivity, also the elevated levels at that point in time have improved the AUC to 0.87 compared

with the final clinical assessment with NRI of 28%, with net improvement in mean predicted probability of +15%.

The combination of clinical judgment and negative interleukin-6 had a sensitivity of 97% with 0nly 2% (8 patients) were classified incorrectly in the urgent group using the combined algorithm, specificity of 93%.

The study has shown some prognostic value for mortality within 180 days, I think this is outside the area of acute abdominal pain as the mortality in this case will depend on the final diagnosis.

I suppose authors could have categorized clinical degree of suspicion into low, intermediate and high rather than the visual analog scale which I find confusing. I also noticed that the cutoff value for interleukin-6 is not clear in the paper as the paper states that median of raised level at 23 ng/L; the negative cutoff was 2.4 ng/L; and in the algorithm the raised levels were considered as more than 63.5 ng/L; I can't see an explanation as how they dealt with levels in between.

The paper states that there were no false positive predictions but we need explanation to the 23 patients who were incorrectly moved upward in the non-urgent group, I would consider that as false positive results which would affect the specificity of the algorithm.

Perhaps the paper is missing a simple table of sensitivity and specificity with likelihood ratios for the algorithm for the two groups of patients because the statistics are two complex and not easy to follow.

We would also appreciate to emphasize more on patients who were misclassified by the test and the potential harm caused by that such as needing further procedures. Although a decision curve analysis was performed but still would benefit from the possible harm calculations.

It would be helpful as well to have a table of those patients who were misclassified by the test as to what diagnosis they ended up having that would be applicable to those with irritable bowel and possibly persistent biliary colic, having said that biliary colic is a real clinical scenario that should not fall in the category of non-urgent pain.

A cost effect analysis is warranted in this case before we can accept that interleukin-6 test should be performed routinely in acute abdominal pain.

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Footnote

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