Ruling in or out a source of gastrointestinal bleeding

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Abstract

Background and aims: The search for a source of gastrointestinal bleeding is associated with two distinct approaches of trying to *rule in* a specific diagnosis or *rule out* any potential source of bleeding. The study aim was to understand the conceptual differences underlying the two searches.

Methods: The performance of endoscopy as diagnostic test is analyzed in terms of Bayes' formula.

Results: The performance of gastrointestinal endoscopy to *rule in* a suspected lesion is mostly influenced by its underlying specificity. Because the specificity of endoscopy is less likely to be affected by procedural exigencies, the demands on pre-procedural prep and general quality can be more relaxed. In contradistinction, the performance of endoscopy to *rule out* a suspected bleeding site is mostly influenced by its sensitivity, which can easily be compromised by suboptimal procedural conditions.

Conclusions: Paradoxically, the more urgent, focused, and important search (to rule in a bleeding site), carries less stringent criteria for its execution than the more general and aimless search (to rule out a bleeding site) that frequently ends up just empty handed.

Keywords

Bayes' formula, gastrointestinal bleeding, gastrointestinal endoscopy, medical decision analysis, outcome research

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Two types of searches for gastrointestinal bleeding sites

The search for a source of gastrointestinal bleeding is one of the most frequent indications for gastrointestinal endoscopy. The endoscopic search is associated with two distinct approaches. The first search serves to *rule in* a suspected diagnosis. The suspicion is usually based on characteristic signs and symptoms, past medical history, clinical presentation, constellation of laboratory parameters, or pre-existing findings on radiologic imaging. The endoscopic search is focused on a single diagnosis or short list of few differential diagnoses ordered by their declining probability of occurrence. Endoscopy serves as a test to confirm a high pre-test suspicion for a specific lesion. The second type of endoscopic search serves to *rule out* any bleeding source inside the gastrointestinal tract. Typical examples relate to patients referred without any specific signs but some laboratory findings suggestive of iron-deficiency anemia. Others patients may report vague histories of “dark” bowel

movements, traces of blood on the toilet paper or a specks of blood observed during a recent episode of vomiting. With such vague presentations it is difficult to a priori assign a high level of suspicion to any specific diagnosis, and the endoscopic work-up serves primarily to make sure that no serious condition becomes missed.

A paradox in the search for bleeding sites

The first type of endoscopic search is frequently associated with emergency procedures done on inpatients or in the intensive care unit. Even if the conditions for such endoscopy are less than ideal and some of the advanced tools of endoscopy may not be available, or

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are less functional, outside the endoscopy suite, the need for speed, expeditious detection and early intervention trumps such concerns. The physician trusts that the endoscopy will be still able to identify and localize the bleeding site even if the patient has not been kept fasted for more than 6–8 hours and remnants of blood are present in the upper gastrointestinal tract, or if the bowel preparation for colonoscopy has not been perfect. The goal of the endoscopic procedure is to identify one specific marker for gastrointestinal bleeding.

The requirements for the second type of endoscopic search are strikingly different. In a general search for some unknown or even unsuspected bleeding site, endoscopists would want the best possible conditions for their search. The upper gastrointestinal tract should be completely empty so that even the most subtle lesions, such as Dieulafoy ulcers, Cameron lesions, or rare hemobilia are readily detected. Similarly, for colonoscopy one would want a perfect bowel prep, to discover subtle lesions and screen a large surface area with multiple niches and folds unencumbered by stool rests or opaque fluid. One would even consider a 2-day rather than 1-day regimen for prepping the bowel, and using a double dose of cleansing solution.

There seems to be a paradox underlying these two sets of different pre-requisites for the two types of endoscopy to rule in or to rule out a source of gastrointestinal bleeding. On one hand, the endoscopy that deals with a potentially life-threatening bleeding type is agreeable to relatively lax conditions. On the other hand, the endoscopy to identify a chronic and mostly non-threatening bleeding demands far more stringent pre-conditions for its execution. Why would the more urgent, focused, and important search carry less stringent criteria than the more general and aimless search that frequently ends up just empty handed?

Sensitive versus specific searches

The discrepancy between the two types of endoscopy to rule in and rule out a bleeding site cannot be explained solely by their varying levels of emergency. It rather reflects on the diagnostic characteristics of endoscopy in general with respect to its sensitivity and specificity. Diagnostics through endoscopy are generally associated with high specificity, as endoscopists rarely err in calling a specific diagnosis. With very few exceptions, an ulcer seen on esophago-gastro-duodenoscopy (EGD) is truly an ulcer, and a cancer seen on colonoscopy is rarely anything else but. Compared with its specificity, however, the sensitivity of any endoscopic diagnosis is less reliable and more dependent on external circumstances. Poor colon prep may do little

to influence the specificity of colonoscopy, but will markedly reduce its sensitivity. Similarly, a stomach filled with blood clots will compromise endoscopists' ability to localize a bleeding site, but leave their ability to correctly identify the lesion's nature unaffected.

The performance of gastrointestinal endoscopy to rule in a suspected lesion is mostly influenced by its underlying specificity. Because the specificity of endoscopy is less likely to be affected by procedural exigencies, the demands on pre-procedural prep and general quality can be more relaxed. In contradistinction, the performance of endoscopy to rule out a suspected bleeding site is mostly influenced by its sensitivity, which can easily be compromised by suboptimal procedural conditions.

Bayes' formula to characterize two types of searches

The performance of endoscopy as diagnostic test can be best captured in terms of Bayes' formula.¹ The formula shown below applies to the scenario when trying to rule in a particular diagnosis. In the formula, P_{pre} represents the pre-procedural probability for a given diagnosis; P_{post} represents the post-procedural probability for the diagnosis after a positive endoscopic test; $sens$ and $spec$ represent endoscopic sensitivity and specificity, respectively.

$$P_{post} = \frac{P_{pre} \cdot sens}{P_{pre} \cdot sens + (1 - P_{pre}) \cdot (1 - spec)}$$

As an example, let's assume $P_{pre} = 20\%$, $sens = 80\%$, and $spec = 95\%$. After a positive endoscopy the probability for a true diagnosis X would change from $P_{pre} = 20\%$ to $P_{post} = 80\%$. Rather than look at a single value of $spec = 95\%$, however, it is more insightful to change its value over broad range between 50% and 100%, as shown by the broken (red) line in the left panel of Figure 1. The variation of the specificity between 50% and 100% changes the post-procedure diagnostic probability (P_{post}) between 29% and 100%, respectively. In the same graph, the full (blue) line represents the influence of varying the sensitivity between 50% and 100% while keeping $P_{pre} = 20\%$ and $spec = 80\%$. The variation of the sensitivity between 50% and 100% changes P_{post} only between 38% and 56%, respectively. Obviously, the endoscopy test to rule in a diagnosis becomes more affected by changes in specificity than sensitivity.

A slightly modified Bayes' formula applies to scenario when trying to rule out a diagnosis, such as gastrointestinal bleeding.¹ P_{pre} again represents the pre-procedural probability for the diagnosis. P_{post}

Figure 1. Left panel: Influence of sensitivity or specificity on disease probability after a *positive* test to *rule in* a particular diagnosis. Right panel: Influence of sensitivity or specificity on disease probability after a *negative* test to *rule out* any diagnosis. (All calculations assumed a starting pre-test probability of 20%. When varying the sensitivity, the specificity was kept constant at 80% and, vice versa, when varying the specificity, the sensitivity was kept constant at 80%.)

represents the remaining post-procedural probability for the diagnosis after a *negative* endoscopy.

$$P_{post} = \frac{P_{pre} \cdot (1 - sens)}{P_{pre} \cdot (1 - sens) + (1 - P_{pre}) \cdot spec}$$

In the right panel of Figure 1, the full (blue) line represents the influence of varying the sensitivity between 50% and 100% on the post-procedural disease probability (P_{post}) while keeping $P_{pre} = 20\%$ and $spec = 80\%$. The broken (red) line represents the influence of varying the specificity between 50% and 100% on P_{post} while keeping $P_{pre} = 20\%$ and $sens = 80\%$. The variation in sensitivity changes P_{post} between 14% and 0%. In other words, the probability of a missed bleeding site after a negative endoscopy drops from 14% to 0%, or the certainty associated with excluding a bleeding site rises from 86% to 100%. The variation in specificity changes P_{post} only between 9% and 5%, that is, the certainty of exclusion increases only slightly from 91% to 95%. In trying to *rule out* a diagnosis, obviously, the endoscopy test becomes more affected by changes in sensitivity than specificity. All calculations in Figure 1 are based on a pre-procedural probability of $P_{pre} = 20\%$. However, similar patterns apply to a broad range of other pre-test probability values that are much higher or lower than 20%.

Clinical implications and outlook

To *rule in* a particular source of gastrointestinal bleeding, one relies on gastrointestinal endoscopy to provide a highly *specific* diagnostic test, whereas to *rule out* any type of gastrointestinal bleeding one wants endoscopy to be the most *sensitive* test possible. There is little that

one can do in the short run to improve endoscopic specificity except, possibly, for good training and extensive experience in identifying a variety of individual lesions. In the long run, however, advances in endoscopic instrumentation and technique could further improve the already high specificity of gastrointestinal endoscopy. Similarly to microendoscopy or chromoendoscopy improving endoscopic specificity in correctly identifying neoplastic lesions, it is conceivable that in the future other technological advances will be able to also increase endoscopic specificity with respect to gastrointestinal bleeding.^{2,3}

In contradistinction with specificity, several relatively simple means already exist to improve endoscopic sensitivity. A good bowel prep and a slow withdrawal of the colonoscope after reaching the cecum are likely to improve general sensitivity for any type of colonic abnormality. Similarly, the use of prokinetic drugs prior to EGD to accelerate gastric emptying and rid the upper gastrointestinal tract of blood clots could potentially improve its overall sensitivity.⁴ In the future, endoscopic sensitivity will also benefit from changes in instrumentation. Full-spectrum endoscopy with increased field of view, or balloon distension to straighten colonic folds may increase detection rates not only of adenoma but also of bleeding sites.^{5,6}

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Conflict of interest

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