Technetium-99m-labeled RBC scintigraphy: unrealised potential, unharnessed power?

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Foot line: Scintigraphy in Acute GIT Bleeding

We thank Dr Tabibian[1] for the comments and interest in our recent article on red blood cell scintigraphy in gastrointestinal haemorrhage[2]. While our intention was not to provide some definitive measure of sensitivity or specificity but rather to provide a very broad introduction, Dr Tabibian draws attention to an important issue. As we discussed in the original article[2], there is significant variability in measures of efficacy and, as demonstrated by Dr Tabibian[1], it is relatively simple to find a handful of articles that report negatively. The number of participants is less important than the methodology, selection of those patients and choice of outcomes measures and 'gold standards' against which to make the evaluations. Nonetheless and outside the scope of the original article, there are a number of pitfalls in attempting to make a comparison of diagnostic yield of the procedures utilised in the evaluation of acute lower gastrointestinal haemorrhage (LGIH):

- To make a determination of diagnostic efficacy one requires a reliable final diagnosis and there are large numbers of patients who remain undiagnosed. Patients with greater blood loss are both more likely to have a positive diagnosis and more likely to undergo surgery (i.e. providing a reliable final diagnosis).
- Sensitivity is the ability to diagnose bleeding when bleeding is present. With the intermittent nature of acute LGIH, it is difficult in the presence of a negative finding to determine whether bleeding was occurring during the procedure. Determining the absolute sensitivity of these procedures is an impossible task and this may be reflected in the extremely variable degrees of success.
- There is no recognised 'gold standard' for detection and localisation of acute LGIH.
- Many authors quote sensitivities for detection of acute LGIH but neglect evaluation of the more important accurate localisation; or confuse the two. Sensitivity and accurate localisation are two different outcome measures.
- Studies tend to be retrospective (rather than prospective), small in patient numbers and employ heterogeneous groups of UGIH / LGIH and acute / chronic bleeding.
- There has been a lack of defined criteria for determining accuracy of localisation.

The ranges for sensitivity and specificity quoted in our article[2] attempted to provide an insight into 'post filtered' reports. That is, a rigorous and systematic approach had been undertaken to eliminate

articles that might have some degree of limitation. Dr Tabibian[1] cites a number of articles (largely retrospective in nature) that require deeper discussion:

- The 'largest' study[3] is well short of being the largest study. While 287 patients are reported in the sample, only 40 patients were actually recruited into the study and this was associated with a selection bias. Indeed, one finds it difficult to accept the validity of the 'gold standard' when a large number of positive studies were 'ignored by the surgeon'[3]. Nonetheless, the study reported 70% sensitivity[3].
- The 'second largest' study reported 51% of patients to be positive for bleeding[4]. This does not translate to sensitivity or imply false negatives. Furthermore, the use of scintigraphy was not random or standard; it was used at the discretion of the clinician[4]. Nonetheless, patients with positive scintigraphy were five times more likely to require surgery than patients with negative scans ($p < 0.005$)[4]. Moreover, 97.3% had correct localization based on surgical pathology[4].
- The 'third largest' study included data collected between 1984 and 1989[5] and was incorrectly reported by Dr Tabibian[1]. The reported 26% of patients that were positive does not reflect sensitivity. It simply indicates that 26% of the patients that presented were detected to be actually bleeding at the time of the scan. In reality, it may well reflect 100% sensitivity if indeed it were measured against a reliable 'gold standard' (which does not exist). Certainly 'inaccurate localisation' does not translate to a false positive. Moreover, their population included acute and chronic bleeders and only 22 patients were considered to have reliable follow-up[5].
- Despite the limitations cited above, the articles referenced by Dr Tabibian provide a positive outlook for the role of scintigraphy in acute LGIH.

Howarth, Tang and Lees[6] used a population of 137 patients presenting with acute LGIH and demonstrated in the 47 patients with a reliable final diagnosis that the overall sensitivity of ^{99m}Tc RBC scintigraphy was 87% for the detection of bleeding but only 54% for the accurate localisation of a bleeding site. Surgical pathology was employed as a confirmatory tool by Suzman et al. [3] to demonstrate a 97.3% localisation accuracy for ^{99m}Tc RBC scintigraphy in acute LGIH. Surgical pathology was also used by Guitierrez et al.[7] to demonstrate an 88% accuracy of localisation in acute LGIH with ^{99m}Tc RBC scintigraphy. The accuracy of localisation was determined to be

somewhat poorer at 72.7% by Rantis et al.[8], however, this may be the result of infrequent and non continuous imaging (5, 15, 30, 40 and 60 minutes) and inclusion of bleeding sites only identified on delayed imaging. An 85% failure rate for accurate localisation of bleeding sites was reported by Voeller, Bunch and Britt[9] which is explained, in part, by their use of *in vivo* blood labelling, non continuous imaging at five minutes intervals and the inclusion of patients with UGIH. Similarly, Garofalo and Abdu[10] reported scintigraphy to be neither accurate nor cost effective due to only 19.3% localisation accuracy and yet again poor techniques were employed (*in vivo* blood labelling and non continuous imaging at 15 minute intervals) and exclusion criteria were not utilised (inclusion of positive studies on delayed imaging and patients with UGIH) rendering the results of questionable clinical value.

Dr Tababian's second paragraph[1] of concerns regarding our paper[2], I would suggest, relates to some degree to the discussion above. The relatively low rate of positivity may well reflect a poor transition time from patient presentation to actual scanning. Delay in starting the procedure (eg. stabilising the patient) will decrease the positivity rate. There is also the issue of selection bias, with an increasing tendency for only the 'tough' patients that have confounded previous examinations being sent to scintigraphy. Frustratingly, a negative study in these circumstances is seen as a failure when, in fact, it is likely to reflect precisely the circumstances at the time of the patient presenting for the test; they were not actually bleeding at the time. Thus, permeation of our recommendations into clinical practice (including our recommendations to provide very good detection and localisation even at slow bleeding rates) require a quantum shift in current patient management. While this requires an open dialogue between the image service provider and the referring clinicians, the point of the article was to provide sufficient detail to allow the referring clinician to drive the requirements; to demand specific conditions in which to examine their patient to maximise diagnostic integrity. Certainly there was sufficient detail in the original article[2] to accommodate patient related factors (eg. subtraction for slower bleeds, to correct for motion, accommodate obesity etc) and the issues relating to patient stabilisation prior to commencement of the procedure (delaying and diminishing diagnostic utility).

Scintigraphy is widely reported as cost effective[11] and non invasive as Dr Tabibian indicated[1]. Assessed on its merits, the procedure is highly accurate[12] and can be made more accurate and

reliable if our recommendations were followed[2,13,14]. The procedure is certainly not associated with the high radiation doses of CT, the risks of contrast, risks of perforation or the narrow window of opportunity for detection. It is well tolerated even in gravely ill patients and actually images the bleed (rather than relying on stigmata or other pathology as evidence of a likely source).

Lack of portability presents some issues for the unstable patients but none that can not be managed and is managed in many centres. Inconvenience should not be prohibitive of performing the optimal procedure and certainly unstable patients are regularly mobilised for CT procedures (mostly CNS injury). If an after hours service is not available and is of deleterious impact on patient management, I am sure an imaging provider would be open to discussion. In Australia, most hospital based nuclear medicine facilities (whether public or private in nature) will provide an on-call service after hours. Nonetheless, regardless of the method of examination (eg. colonoscopy, CT etc), after hours access will present an issue so it is unclear why it is only prohibitive for scintigraphy. Indeed, scintigraphy can be performed with minimal expertise (technical staff with medico reporting remotely from home if need be) while a larger team and more expert medicos are required for colonoscopy and CT contrast administration.

The onus, I would think, is on the referring clinicians (not the nuclear medicine specialists). Certainly that was the point of the article; to arm the clinicians with the actual capabilities of the procedure so decisions can be made on how best the technology meets the management needs of their patients and, indeed, to recognise circumstances when scintigraphy is unlikely to be useful.

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