

ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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Update on the Use of Capsule Endoscopy

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G&H Could you briefly outline how capsule endoscopy procedures are performed?

KM In small-bowel capsule endoscopy, the patient swallows an apparatus that essentially looks like a large vitamin pill and contains a camera, light sources, and 2 batteries. As the capsule passes through the gastrointestinal (GI) tract, it captures 2 pictures per second, which are sent by a radio transmitter to a recorder that the patient wears on a belt. A number of electrodes are attached to the patient's abdomen, similar to long-term electrocardiogram techniques. The procedure is performed passively; as the gastroenterologist cannot steer the capsule, it photographs whatever it encounters as it passes from the stomach through the large intestine. After 8 hours, the batteries in the capsule become depleted, ending the examination. At a rate of 2 images per second for 8 hours, more than 55,000 images are captured and transmitted to the recorder, which acts as a portable hard drive. Proprietary software from the capsule manufacturer "glues" those images into a video, which is then downloaded onto a computer. The gastroenterologist can review the video for abnormalities by running it forward, backward, fast-forward, single-image forward, single-image backward, and so on.

G&H What are the different types of capsules used, and what are their primary applications?

KM There are currently three types of capsules and capsule examinations, one for each segment of the intestine, that are either being studied or are already on the market. The first capsule approved by the US Food and Drug Administration (FDA), in 2001, was the small-bowel cap-

sule. The second type of capsule, the esophageal capsule, was approved by the US FDA in 2004. A third type, the colon capsule, is still in the early stages of development and has not yet been approved by the US FDA. Small-bowel capsule endoscopy currently accounts for more than 90% of all capsule examinations performed in the United States.

The main indication of the small-bowel capsule is in cases of obscure GI bleeding with a suspected source in the small bowel. I believe that this will remain the main indication for a long time; in my own practice, it makes up more than 90% of all small-bowel capsule examinations. A second indication for the small-bowel capsule involves a subgroup of patients with suspected Crohn's disease, in whom conventional examinations for Crohn's disease have not yielded a definitive diagnosis. This can occur when the inflammatory changes of Crohn's disease are limited to a segment of small bowel that cannot be reached with conventional endoscopes. In these cases, capsule endoscopy may detect these abnormalities and help make the diagnosis.

It has also been suggested that small-bowel capsule endoscopy can be useful in patients with celiac disease; known Crohn's disease, for an assessment of disease severity; and possibly even in the evaluation of patients with diarrhea or abdominal pain of unclear etiology. However, there have not been any definitive studies demonstrating that capsule endoscopy has an important role to play in the majority of these patients. Its use in these cases should be individualized and generally discouraged.

The esophageal capsule is currently being marketed for two indications. One indication is the detection of esophageal varices in patients with liver disease, as the varices in these patients can cause complications by bursting and bleeding. Currently, the standard of care is to screen patients with certain types of liver diseases or

known varices, and it has been suggested that rather than perform these screening examinations with conventional endoscopes and sedation that screening be performed in a less invasive fashion using the esophageal capsule. The second indication is for detecting Barrett esophagus in patients with longstanding gastroesophageal reflux disease. Current practice guidelines recommend conventional endoscopy in these patients to screen for Barrett esophagus, which is known to predispose patients to developing esophageal cancer. As with varices, some gastroenterologists have suggested that the use of capsule endoscopy may increase patient acceptance of such screening procedures because capsule endoscopy is less invasive and does not require sedation.

G&H How did capsule endoscopy become so widely adopted so quickly?

KM Usually, it takes a long time for a new technology to become accepted in the medical community. Small-bowel capsule endoscopy took off very quickly after FDA approval in 2001 because it filled an important void. Prior to 2001, there was no way of directly visualizing most of the small-bowel mucosa except with various radiographic studies that were inadequate for detecting small abnormalities such as angioectasias, small erosions, or inflammatory changes. The second reason that capsule endoscopy was adopted so quickly relates to the fact that it is relatively easy to administer. The patient simply swallows a capsule; they do not need to undergo an inpatient procedure, swallow a large tube, be sedated, or undergo an unpleasant bowel preparation process such as the one used for colonoscopy.

In addition, with this examination, the gastroenterologist does not need to acquire a set of technical skills, as is the case with conventional endoscopy. Rather, the learning curve for capsule endoscopy relates to the ability to recognize mucosal abnormalities on the basis of merely a few images of poorly distended bowel on a computer screen, without the opportunity to biopsy, flush, change the position of the endoscope, or otherwise improve the image. Making a confident diagnosis under these circumstances can initially be challenging even for gastroenterologists with considerable experience in conventional endoscopy.

G&H What has recent research suggested regarding the sensitivity, specificity, and diagnostic yield of the small-bowel capsule compared to other endoscopic options?

KM There has been a number of studies comparing small-bowel capsule endoscopy to small-bowel follow-through

radiographs. Unsurprisingly, capsule endoscopy was found to be more sensitive in detecting most small-bowel abnormalities. Early studies comparing capsule endoscopy to push enteroscopy, a conventional endoscopic examination of the proximal small bowel using long endoscopes, found that capsule endoscopy was most likely as good as conventional endoscopy for detecting abnormalities in the first few feet of small bowel. It should be noted, however, that none of these comparison studies were conducted on a particularly large scale and all of them were missing a definitive gold standard.

Because of this lack of a gold standard, it has been difficult to determine the true sensitivity of capsule endoscopy for the detection of small-bowel lesions. Large case series have consistently reported that abnormalities are detected in approximately 50–70% of patients undergoing small-bowel capsule endoscopy. However, it is possible that these studies overestimate the true yield of capsule endoscopy in clinical practice because of methodologic problems with patient selection and the definition of clinically relevant findings. Many of the early trials counted any detected abnormality as a positive finding even if some of the abnormalities (such as a tiny red spot in an otherwise normal small bowel) may have been of questionable clinical relevance. Case series without appropriate controls or gold standards leave gastroenterologists with some uncertainty as to the true accuracy of capsule examinations. Comparison trials with newer endoscopic technologies such as double-balloon enteroscopy, which theoretically allows visualization of the entire small bowel, may soon serve to answer some of these questions regarding the test characteristics of capsule endoscopy.

G&H What data have researchers recently reported regarding the sensitivity and specificity of the esophageal capsule?

KM For its two indications, varices and Barrett esophagus, I believe that it is too early to determine whether the esophageal capsule can eventually replace conventional endoscopy on a broad scale. Conventional endoscopy works very well for these indications and allows gastroenterologists to flush, suction, and biopsy, which the capsule currently does not. Interestingly, initial studies of the esophageal capsule compared to conventional endoscopy showed very positive results, with sensitivities upwards of 90–95% for detecting varices or Barrett esophagus. Subsequent trials, however, have been less encouraging. For example, with a group of other gastroenterologists, I recently published a blinded comparison of esophageal capsule endoscopy versus conventional endoscopy for the diagnosis of Barrett esophagus in patients with chronic gastroesophageal reflux and found that approximately one

third of all Barrett cases were missed by the capsule. Most gastroenterologists would consider this an unacceptably high miss rate. These results were confirmed by another trial, conducted by a group of French investigators, which was published in the January 2008 issue of the *American Journal of Gastroenterology*. Although methodologic differences may account for some of the discrepancies in the results between the various trials, the true accuracy of esophageal capsule endoscopy remains somewhat unclear at this time and needs to be studied further.

G&H Are there cost-effectiveness data on capsule endoscopy versus other forms of endoscopy?

KM Several studies have examined the cost-effectiveness of small-bowel and esophageal capsule endoscopy. However, in the absence of large-scale prospective trials, any study using a retrospective design or modeling technique must be interpreted with caution because the results of such studies are largely dependent upon the quality of the data entered and the accuracy of the initial assumptions. With the test characteristics of capsule endoscopy still somewhat uncertain (as discussed above), any such cost-effectiveness study is difficult to interpret.

Keeping these limitations in mind, it has been suggested by several authors that small-bowel capsule endoscopy leads to substantial cost savings by identifying small-bowel bleeding sources in a significant number of patients, thereby directing them to appropriate treatment and decreasing the rate of costly clinic visits and hospitalizations.

The cost utility of esophageal capsule endoscopy for the screening of Barrett esophagus is very much in question, with several recent analyses suggesting that an initial conventional endoscopy appears more effective and less costly.

G&H Are there any other limitations or disadvantages in the use of capsule endoscopy, as compared to conventional endoscopy?

KM You can steer a conventional endoscope, which you cannot currently do with capsule endoscopy, as mentioned above. Another disadvantage of capsule endoscopy is that, unlike conventional endoscopy, you cannot flush or suction anything that interferes with the visualization of the lining of the GI tract, such as secretions, bubbles, particulate matter, or medication particles. Lastly, it is not possible to obtain samples via capsule endoscopy. If the capsule identifies an abnormality, the gastroenterologist will not know until the video is reviewed, usually at least several hours later. The gastroenterologist cannot stop the

capsule, extend a biopsy forceps, and obtain a sample. Thus, the gastroenterologist is relying solely on visual cues to make a diagnosis. There is more diagnostic uncertainty in capsule endoscopy than in conventional endoscopy.

G&H Are there any adverse events or other concerns that can be related to capsule endoscopy?

KM The main risk of performing capsule endoscopy is capsule retention, particularly if a patient has a stricture from prior surgery or Crohn's disease. If capsule retention occurs, the device must be removed surgically, as it contains metallic batteries and could cause a perforation. (There has been at least 1 case report of bowel perforation as a result of an impacted capsule.) Because of the risk of capsule retention, gastroenterologists usually avoid performing capsule endoscopy if they suspect that the patient may have a stricture. In this situation, it may be preferable to first perform a small-bowel radiograph to better define the anatomy, even though these radiographs have been shown to sometimes miss strictures. A dissolvable capsule is available and can be used in patients with suspected strictures to probe for the presence of significant intestinal narrowing before proceeding with the standard capsule examination.

Capsule endoscopy is a tremendously valuable examination, but it is not a panacea for detecting small-bowel abnormalities. It is very helpful, but it needs to be used in conjunction with other studies with the patient's overall clinical status in mind. Capsule endoscopy can be very easily overutilized, as it is easy to administer and it is not invasive. For example, a 95-year-old woman with multiple medical problems who is not a candidate for surgery or invasive endoscopic techniques is unlikely to benefit from capsule endoscopy performed for stable anemia even if the capsule were to detect a small-bowel angioectasia. Except in unusual circumstances, a capsule examination, like any other diagnostic study, should only be administered if it is likely to affect the management of the patient's clinical problems.

G&H Have there been any recent advances in the design or use of capsule endoscopy?

KM The development of these capsule devices has been a stunning technical success from the very beginning. Even the first generation of capsules in 2001 had excellent imaging capabilities. There has been a steady stream of technical improvements since then. The light sources and camera angle have been optimized. The battery life has been improved. The software used to read and interpret capsule studies has been made more user-friendly. There

are now two companies manufacturing capsule devices, which promotes competition and further innovation. New features, such as a real-time viewer, have been added to the capsule recorder and may pave the way for new indications in patients with active gastrointestinal bleeding. Research into ways of making these capsules steerable and adding biopsy and sampling capabilities is also ongoing.

In addition, the colon capsule is now undergoing clinical trials. The results of these studies are eagerly awaited to see if capsule devices may find a role in the screening for colon cancer.

Suggested Reading

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