Capsule Endoscopy To Screen for Colon Cancer Scores Low on Sensitivity, High on Controversy

By Charlie Schmidt

Nobody looks forward to a colonoscopy, so a more convenient and noninvasive alternative might boost colorectal cancer screening rates—or so the argument goes. One such alternative is capsule endoscopy. Patients who undergo this procedure swallow a disposable capsule outfitted with a pair of cameras and a wireless transmitter. The device, known as PillCam, shoots roughly 50,000 images during a trip through the colon. Those images are collected by an external recorder and then compressed by software into a diagnostic video.

PillCam’s ability to detect colon polyps or cancer doesn’t compare well to that of colonoscopy, however. And because of that, its use for cancer screening remains controversial. The method has regulatory approval in countries in Europe, Asia, and Latin America, according to its manufacturer, Given Imaging, in Yokneam, Israel. But health systems don’t pay the $1,150 cost even in these countries, said Michael Bretthauer, M.D., Ph.D., an editorial fellow at the New England Journal of Medicine who is currently on leave from Rikshospitalet University Hospital in Norway. PillCam was denied approval by the U.S. Food and Drug Administration in February 2008.

Now, the results of a European multicenter study comparing PillCam and colonoscopy, published in the New England Journal of Medicine in July, are further dividing gastroenterologists. PillCam’s sensitivity—or its ability to detect polyps that were also detected by colonoscopy—averaged just 42% among subjects with poor bowel preparation and 72% for those with good to excellent preparation. In all, PillCam identified 14 of 19 malignant tumors revealed by colonoscopy, and it often missed larger polyps in excess of 10 mm, which can easily progress to cancer.

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The study’s lead author, Andre Van Gossum, M.D., from Erasme University Hospital, in Brussels, claims the results are more encouraging than might be reflected in the report. In Van Gossum’s view, clinicians are only now gaining experience with the capsule, which he believes will improve with technical advancements.

But in an accompanying editorial, and during interviews for this article, Bretthauer countered that PillCam’s performance is unavoidably limited by feces remaining in the colon even after extensive bowel preparation. This material, Bretthauer said—which clinicians can aspirate and remove during colonoscopy—obscures the camera’s view of potentially dangerous lesions.

Bretthauer said fecal obstructions in the colon will always undermine technical improvements to the capsule. “I just don’t know how you get around that,” he said. “You’ll never get 100% cleansing and the cameras just can’t see through all that brown fluid.”

Technical Improvements

Van Gossum claimed that better cleaning protocols can be devised, and he added that PillCam’s performance can be improved further by increasing its “frame speed,” or the rate at which it gathers images. The recently tested capsule takes four pictures per second—two each per camera—which doesn’t always keep pace with PillCam’s speed through the colon. The company has since introduced a second-generation capsule with a higher frame speed.

PillCam is not the first capsule to be used for bowel screening. Given Imaging won FDA approval for a small-bowel capsule in 2000, used mainly to screen for obscure gastrointestinal bleeding and suspected Crohn disease, according to chief
executive officer Homi Shamir. But capsule endoscopy in the small bowel is straightforward compared with colon screening: The small bowel presents no fecal obstructions or secretions to contend with after preparation. Moreover, the small bowel’s narrow lumen propels a capsule forward in one direction, such that only one camera, mounted on the device’s front end, is required for imaging. The colon’s lumen, on the other hand, is much wider, and within it, PillCam tumbles randomly. To maximize surveillance during this turbulent passage, the colon capsule was outfitted with two cameras, Shamir said, one pointing forward and another pointing backward.

Even with these modifications, the capsule often missed regions of the colon when it was traveling too fast, Gossum said. Given Imaging’s second-generation PillCam, now being tested in a multicenter Israeli study, aims to avoid that problem by taking up to 30 frames per second with cameras that pause when the capsule stops moving.

Bretthauer said he doubts the higher frame speed will make a difference in performance, but both Van Gossum and Douglas Rex, M.D., director of endoscopy at Indiana University Hospital in Indianapolis, believe it might. “Frame speed is almost certainly an issue,” Rex said. “The capsule travels in jerky movements and there isn’t always a seamless transition from one image to another.”

**Colon Cleansing**

But frame speed problems are minor compared with inadequate cleansing, Rex said. In addition to residual feces, the colon’s internal membranes secrete mucosal flecks that wind up suspended in fluid. And those flecks increase fluid turbidity in the colon and further obscure the camera’s view. “You need a way to disperse that mucus before the capsule’s sensitivity can be substantially improved,” said Rex, who has served on Given Imaging’s advisory board.

According to Bretthauer, the cleansing regimen used during the European multicenter study is arguably twice as arduous as that used in colonoscopy, in part because substantial fluidity is needed to propel the capsule through the colon. Both approaches require patients to drink 4 L of polyethylene glycol, a laxative, within 24 hours of the procedure. But patients undergoing capsule endoscopy also had to take a drug called domperidone, which helps draw food into the large intestine (it is sometimes used to prevent vomiting); two 45-mL bottles of phosphosoda, an over-the-counter laxative; and another laxative called bisacodyl, given as a rectal suppository.

Bretthauer said many patients who decline colonoscopy do so to avoid the preparation more than the procedure, which they can undergo while sedated. If capsule endoscopy requires even more preparation, he asked, why would patients choose it over colonoscopy, which offers better screening results and the opportunity to remove polyps as they’re found?

Samuel Adler, M.D., chief of gastroenterology at Bikur Holim Hospital in Jerusalem, and a principal investigator studying Given Imaging’s second-generation capsule, responded that the existing preparation protocol has been simplified, though it still relies on 4 L of polyethylene glycol and phosphosoda as a booster. “My personal experience has been that bowel preparation for capsule endoscopy is now subjectively superior,” he said. “I no longer have cases in which I feel the bowel preparation is inadequate, whereas in prior studies with the capsule I had many cases like that.”

Adler didn’t mention convenience, but proponents of another noninvasive alternative to colonoscopy, CT (computed tomography) colonoscopy, or virtual colonoscopy, do cite this advantage: Patients undergoing virtual colonoscopy, which uses CT scans to look for polyps, don’t need to be sedated and don’t need to arrange for someone to take them home, in contrast to colonoscopy (see News, J. Natl. Cancer Inst. 2008;100:1492–9). PillCam, which the patient can swallow at home and then deliver to the doctor’s office, could be even more convenient.

Adler also pointed out that the capsule’s negative predictive value, or ability to discern the absence of polyps and cancer correctly, is near 90%. This value does not appear in the *New England Journal of Medicine* article, but Van Gossum confirmed it.

**Noncompliant Population**

Still, it’s misguided to compare colonoscopy and capsule endoscopy on an apples-to-apples basis, Adler said. He acknowledged that colonoscopy is the better option for those who agree to it. But he argued that capsule endoscopy offers at least some screening value for the noncompliant population that refuses the procedure. “What are we supposed to do, just write the noncompliant population off? Or do we tell them, ‘Look, here’s a weekend procedure you can do at home. Just return the recorder, and if you don’t have polyps, we’ll be able to tell you that with nearly 90% certainty.’”

According to Adler, compliance rates for colonoscopy vary widely by country. In Israel, just 20% of the eligible population gets colonoscopy, he said, although the rates appear to be rising. Bretthauer said that compliance rates in southern Europe average 20%–30%, whereas they range up to 80% in northern Europe and the United States. Rex added that shortages of trained personnel and the procedure’s high cost limit colonoscopy’s adoption in some countries, particularly in southern and eastern Europe, where capsule endoscopy has been heavily marketed.

Bretthauer acknowledged the problem of noncompliance but still advocates caution. “To be fair, many patients don’t like colonoscopy, so generally speaking if more patients would accept the capsule and get the screening done, that might be a good thing for society in terms of minimizing cancer death,” he said. “But we have to note that this tool is [substantially] poorer than colonoscopy, and it’s also too expensive.”

Marketing capsule endoscopy on the same footing as colonoscopy is the wrong approach, he added. “If we recommend it to our patients, we also have to tell them that it’s not as good as the ‘gold standard.’”

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