

Medical Policy Manual

Topic: Ingestible pH and Pressure Capsule

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Section: Medicine

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

An ingestible pH and pressure-sensing capsule (SmartPill® GI Monitoring System) is proposed as a means of evaluating gastric emptying and small bowel, colonic, and whole gut transit times. This technology is used to evaluate suspected gastrointestinal motility disorders such as gastroparesis, intestinal dysmotility, and slow-transit constipation. The ingestible pH and pressure capsule, which may also be referred to as a wireless motility capsule, measures pH, pressure, and temperature changes to signify passage of the capsule through portions of the gastrointestinal tract. For example, an increase of 2 or more pH units usually indicates gastric emptying, and a subsequent decrease of 1 or more pH units usually indicates passage to the ileocecal junction. This differs from esophageal pH monitoring for gastroesophageal reflux disease which measures pH levels in various ways such as through catheters, impedance or a temporarily implanted device such as the Bravo. The ingestible pH and pressure capsule also differs from the wireless capsule endoscopy (i.e., PillCam™) which is a capsule swallowed by the patient that transmits video images wirelessly.

Gastroparesis is a chronic disorder characterized by delayed gastric emptying in the absence of mechanical obstruction. Symptoms of gastroparesis are often nonspecific and may mimic other gastrointestinal disorders. It can be caused by many conditions; most commonly it is idiopathic, diabetic or postsurgical. The test considered the reference standard for gastroparesis is called gastric emptying scintigraphy. The patient ingests a radionuclide-labeled standard meal, and then images are performed at

0, 1, 2, and 4 hours postprandially to measure how much of the meal has passed beyond the stomach. A typical threshold to indicate abnormal gastric emptying is more than 10% of the meal remaining at 4 hours after ingestion.

Many patients with gastroparesis or symptoms of gastroparesis also have coexisting lower gut involvement. Testing for small and large bowel motility disorders includes manometry, colonic transit study, whole gut or colonic transit scintigraphy, radio-opaque markers, and orocecal breath tests. These tests are often used in combination to assess symptoms of gastrointestinal dysmotility and for diagnostic evaluation.

Regulatory Status

In 2006 an ingestible capsule (SmartPill® GI Monitoring System) was cleared for marketing by the U.S. Food and Drug Administration (FDA) via a 510(k) application with the indication for use in adult patients to evaluate delayed gastric emptying. Gastric emptying is signaled when the pH monitor in the capsule indicates a change in pH from the acidic environment of the stomach to the alkaline environment of the small intestine. While SmartPill does not measure 50% emptying time, it can be correlated with scintigraphically measured 50% emptying time. The capsule also measures pressure and temperature throughout its transit through the entire gastrointestinal (GI) tract, allowing calculations of total GI transit time.

In 2009 the FDA expanded the use of the SmartPill to determine colonic transit time for the evaluation of chronic constipation and to differentiate between slow versus normal transit constipation in adults. When colonic transit time cannot be determined, small and large bowel transit times combined can be used instead.

The SmartPill is not for use in pediatric patients.

Note: This policy does not address wireless capsule endoscopy which is addressed separately in [Radiology, Policy No. 38](#), or esophageal pH monitoring which may be considered medically necessary.

MEDICAL POLICY CRITERIA

Measurement of gastrointestinal transit times including gastric emptying and colonic transit times using an ingestible pH and pressure capsule is considered **investigational** for all indications, including but not limited to suspected gastroparesis, constipation, or other gastrointestinal motility disorders.

SCIENTIFIC EVIDENCE^[1]

Evaluation of a diagnostic technology typically focuses on the following three parameters:

- Technical performance is evaluated by comparing test measurements with a gold standard.
- Diagnostic performance (i.e., sensitivity, specificity, and positive and negative predictive value) is evaluated by the ability of a test to accurately predict the clinical outcome in appropriate populations of patients. The sensitivity of a test is the ability to detect a disease when the condition is present

(true positive). The specificity is the ability to detect the absence of a disease or outcome when the disease is not present (true negative).

- Clinical utility is a key aspect in evaluating clinical test performance. Clinical utility is based on demonstration that the diagnostic information can be used to improve patient outcomes.

Additionally, when considering invasive monitoring, any improvements in patient outcomes must be outweighed by device-related risks associated with testing.

Literature Appraisal

Diagnostic Accuracy of Wireless Pressure and pH Capsule

Gastric Emptying

Although gastric emptying scintigraphy is considered the reference standard for evaluating gastric emptying, several issues complicate its use as a reference test. Until recently, there has been a lack of standardization of the test.^[2] Differences in the test meal used, patient positioning, frequency, duration, and interpretation of imaging all limit the clinical utility of the test. Significant day-to-day variability in the rate of gastric emptying has been noted.^[3]

There is limited knowledge regarding the capability of the gastric emptying test to discriminate between healthy individuals and those with known gastroparesis due to lack of standardization of the test and small patient samples in published studies. One study, which proposed a threshold of normality at 10% meal retention at 4 hours, included only 123 healthy subjects.^[4] The cutoff point was set to include 95% of normal persons. However, it appears to be unknown if this same threshold adequately identifies persons who would otherwise be classified as having gastroparesis and who are candidates or responders to treatment.

Few published studies have evaluated the ingestible capsule in relation to another measure of gastric emptying.

- Cassilly and colleagues evaluated the SmartPill and simultaneous gastric emptying scintigraphy in 15 healthy subjects.^[5] The capsule was ingested immediately after ingesting the radiolabeled test meal. In this study, the mean time for 50% gastric emptying by scintigraphy was 95 minutes, 90% gastric emptying by scintigraphy was 194 minutes, and gastric residence time by SmartPill was 261 minutes. The correlation of SmartPill to 50% gastric emptying time was 0.606 and to 90% gastric emptying time was 0.565. The average amount of meal remaining in the stomach at the time the SmartPill exited the stomach was 5.4%. This study only shows modest correlation of the SmartPill and gastric emptying scintigraphy. The study is too small to establish reference values for the SmartPill.
- Kuo and colleagues evaluated 87 healthy subjects and 61 subjects with symptoms and prior positive test results for gastroparesis using both the SmartPill and gastric emptying scintigraphy.^[6] In this study, subjects ingested the capsule just before ingesting the standard meal. This resulted in 5 subjects who passed the SmartPill in less than 30 minutes, who were then subsequently considered to have invalid tests. Sixteen other subjects had equipment malfunctions, and 2 others dropped out. Among the remaining 125 subjects, the correlation of SmartPill emptying time and scintigraphy at 2 hours was 0.63, and between SmartPill emptying time and scintigraphy at 4 hours was 0.73. In terms of the capability to discriminate between gastroparetic patients and healthy subjects, the area under

the curve (AUC) was 0.83 for SmartPill, 0.82 for scintigraphy at 4 hours, and 0.79 for scintigraphy at 2 hours (all $p > 0.05$ for statistical significance), indicating similar capability for discriminating between the two patient groups. At a cutoff point of 300 minutes for the SmartPill, which was established by calculating the ideal cutoff point from the data, the sensitivity was 65% and specificity was 87%. The sensitivity and specificity for scintigraphy using an established cutoff point from the literature of 10% at 4 hours was 44% and 93%.

- Maqbool et al. assessed SmartPill and gastric emptying scintigraphy in 10 healthy asymptomatic subjects.^[7] Emptying time assessed by SmartPill was correlated with the percent meal retained at 2 and 4 hours. The correlation between SmartPill and 2-hour scintigraphy was 0.95. The correlation between SmartPill and 4-hour scintigraphy was 0.70

These data have several shortcomings regarding the use of the SmartPill in diagnosing gastroparesis, and as a result, the diagnostic accuracy is not well defined.

- All of the studies include healthy asymptomatic subjects either entirely or as part of a control group. Healthy subjects do not represent the clinically relevant group under consideration for a diagnosis of delayed gastric emptying. The relevant population of subjects should have symptoms or are being considered for the diagnosis of gastroparesis.
- Because of the change in the protocol for use of the SmartPill from ingesting the capsule before the standard meal to after the standard meal to avoid fast exit of the SmartPill from the stomach, the results of Kuo and colleagues may no longer represent the performance of the device as it is now intended to be used. The cutoff point for sensitivity and specificity was not prespecified; using visual inspection to identify a cutoff point overestimates the diagnostic characteristics of the test.
- Although there was moderate correlation between SmartPill gastric emptying time and scintigraphy, the current reference test, scintigraphy is an imperfect gold standard with limited reliability. This creates difficulties in defining the sensitivity and specificity of SmartPill
- Although overall, the AUCs between the SmartPill and scintigraphy were similar, the modest correlation between the two tests means that there are often discordant results. What such discordant results mean in terms of diagnosis and treatment are uncertain.

Colon Transit Time

Three studies assessed the use of the device for the purpose of measuring colon transit times.

- In the study by Maqbool et al., healthy asymptomatic individuals underwent simultaneous whole-gut scintigraphy and SmartPill assessment of whole gut transit times.^[7] The two techniques correlated with each other reasonably well.
- In another study by Rao et al., normal subjects and subjects with constipation had whole gut transit times assessed with radio-opaque markers and the SmartPill.^[8] The diagnostic accuracy of the two techniques in differentiating the two groups of patients was similar.
- In 2010, Camilleri and colleagues compared the wireless motility capsule to radio-opaque markers in 158 patients with chronic functional constipation.^[9] In this multicenter validation study, the authors reported positive percent agreement between the wireless motility capsule and radio-opaque markers was approximately 80% for colon transit time and small and large bowel transit time. No serious adverse events occurred in the study.

Although these studies show moderate correlations between SmartPill and other methods for assessing colonic transit times, the studies had several shortcomings. Two of the studies included healthy subjects,

who are not the appropriate subjects for evaluating a diagnostic test. The studies did not identify a set of subjects with known slow-transit constipation, which is the clinically relevant subset of patients with constipation that the test should identify. Thus, the diagnostic characteristics of SmartPill for detecting slow-transit constipation are unknown.

Clinical Utility of Wireless Pressure Capsule

Demonstration of clinical utility requires that the technology be associated with change(s) in clinical management that lead to improved health outcomes. The evidence on the clinical utility of wireless pressure capsule is very limited, consisting of two retrospective analyses.

- In 83 patients evaluated for gastroparesis, small intestinal dysmotility and constipation, Kuo and colleagues found wireless motility capsule testing resulted in a new diagnosis in 44 patients (53%).^[10] Clinical management changes were recommended in 65 patients. These included changes in medication regimens in 39 patients (60%) and in nutrition programs in 9 patients (13.8%). Four patients (6.2%) were referred to surgery for colectomy. Abnormal gastric emptying or small intestinal transit times did not influence patient management at all ($p=NS$). Abnormal colon transit times did not influence nutritional program changes ($p=0.72$) but did influence medication changes ($p=0.02$) and resulted in a trend toward increased surgical referrals ($p=0.12$). The authors believe wireless motility capsule testing eliminated the need for nuclear gastric emptying testing in 9 of 52 patients (17.3%), barium radiography testing in 7 of 13 patients (53.8%), and radio-opaque marker testing in 41 of 60 patients (68.3%). The authors noted a need for prospective studies to further understand wireless motility capsule testing and its role in patient management.
- In 86 patients with persistent symptoms of gastrointestinal dysmotility, despite normal endoscopic and radiologic test results, Rao and colleagues found evaluations with wireless motility capsule testing resulted in new diagnostic information in 26 of 50 patients (53%) with lower gastrointestinal symptoms (LGI) and 17 of 36 patients (47%) with upper gastrointestinal symptoms (UGI).^[11] Clinical management was influenced by wireless motility capsule testing in 30% of patients with LGI symptoms and in 50% of patients with UGI symptoms. The authors indicated the retrospective nature of this study limited interpretation of results.

Adverse Effects

In terms of adverse events reported in the study by Kuo and colleagues, 5 subjects of 67 who did not retrieve the capsule required a second additional plain x-ray beyond 5 days to demonstrate that the capsule had been passed. Another patient had ingested a laxative that caused the capsule to be entrapped in a viscous mass. An unsuccessful endoscopy and treatment with intravenous erythromycin was required to pass the capsule from the stomach.

The U.S. Food and Drug Administration (FDA) has received two adverse event reports.^[12] In the first event, the capsule was trapped in the patient's ileum and required hospitalization with NG tube, IV fluids, and bedrest. In the second event, the patient vomited and choked on the capsule three days after ingestion, requiring performance of self-administered abdominal thrusts to dislodge the capsule. Other reported adverse events included entrapment of the capsule in the esophagus, stomach, and small intestine, some requiring endoscopic removal.

Clinical Practice Guidelines

There are currently no evidence-based clinical practice guidelines from U.S. professional associations that recommend the use of ingestible pH and pressure capsules for any indication.

Three consensus-based position statements have been published, all of which note the lack of sufficient evidence on the impact of the technology on patient management and health outcomes.^[13-15]

Summary

Overall, the data are scant regarding the diagnostic performance and clinical utility of ingestible pH and pressure capsules (i.e., SmartPill® GI Monitoring System) to evaluate gastric emptying time and colon transit time. The evidence to date on technical and diagnostic performance and the clinical utility of this testing consists of a small number of studies that do not provide sufficient information to determine whether health outcomes are improved as a result of the information provided by the SmartPill. Since the impact of measurements using ingestible pH and pressure capsules on net health outcome is unknown, this technology is considered investigational.

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CROSS REFERENCES

[Wireless Capsule Endoscopy as a Diagnostic Technique in Disorders of the Esophagus, Small Bowel, and Colon](#), Radiology, Policy No. 38

CODES	NUMBER	DESCRIPTION
CPT	91112	Gastrointestinal transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report
HCPCS	None	