Is a 15-Minute Collection of Duodenal Secretions After Secretin Stimulation Sufficient to Diagnose Chronic Pancreatitis?

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Background: Standard hormonal stimulation tests of pancreatic function use a 60- to 90-minute collection of pancreatic secretions. A shorter 15-minute collection time has been proposed to increase the feasibility of the secretin stimulation test. The accuracy of this brief collection period for the diagnosis of chronic pancreatitis has not been well defined.

Methods: We retrospectively evaluated the accuracy of a 15-minute collection period by comparing the results of 633 complete standard secretin tests (60 minutes) to the result using only the first 15-minute collection of the same test. The gold standard used for the diagnosis of chronic pancreatitis was the final result of the complete 60-minute secretin stimulation test.

Results: The specificity of the first 15-minute collection was 34.6% (95% CI, 30.03%–39.21%). The positive predictive value was 44.9% (95% CI, 40.5%–49.3%). The accuracy was 57.3% (95% CI, 53.01% 59.34%).

Conclusions: Using only the first 15-minute collection period in a standard 60-minute secretin test is inaccurate in the diagnosis of chronic pancreatitis.

Key Words: secretin stimulation test, chronic pancreatitis

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The diagnosis of chronic pancreatitis is based on the detection of abnormal structure or function of the diseased pancreas. The most accurate way to evaluate pancreatic function is the administration of a hormone stimulation test such as the secretin stimulation test. The reliability of the secretin stimulation test in detecting chronic pancreatitis has been evaluated against histology in more than 100 patients by Hayakawa et al.[1] In this study, the peak bicarbonate (HCO_3^-) concentration of pancreatic secretion was the most accurate parameter for the diagnosis of chronic pancreatitis. Our extensive clinical experience with the secretin test at the University of Florida also indicates that the peak bicarbonate concentration is the best parameter to evaluate.

Although the secretin stimulation test has been accepted as the most sensitive and specific test to diagnose pancreatic exocrine insufficiency, it is not currently widely used.[2,3] The procedure is labor and time intensive and requires trained personnel and a designated laboratory. A passage of a large (26-French) oroduodenal tube is required. The tube has to remain in place for more than 1 hour because the standard secretin stimulation test requires collection of pancreatic secretions for 60 minutes after injection with secretin. During the insertion of the tube and during sample collection, sedation is not used because it may interfere with the test results.[3] The lack of sedation makes the performance of the secretin stimulation test uncomfortable for patients. The degree of discomfort is usually not great, but occasionally a patient may not tolerate the test. One proposed way to improve the feasibility of the secretin stimulation test is a shorter collection time. Some authors have suggested a 15-minute collection of pancreatic secretions instead of the standard 60 minutes.[5] Collection of pancreatic secretion can be accomplished with a standard oroduodenal tube, intraductal placement of a catheter at the time of endoscopic retrograde cholangiopancreatography (ERCP), standard endoscopy, or transnasal passage of small-caliber endoscope.[6–8] It has been standard practice during the performance of the intraductal secretin test at the time of ERCP to evaluate a period of 15 minutes or shorter. It has not been desirable to leave a catheter in the pancreatic duct for a long period of time.

The availability of synthetic porcine secretin and soon-to-be-available synthetic human secretin and the increased appreciation that painful small duct chronic pancreatitis may be detected by the secretin test in the setting of normal radiographic tests (computed tomography, ERCP, endoscopic ultrasound). It is probable that the secretin test will be used more frequently via many different techniques.[9]

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The diagnostic accuracy of 15-minute collection of pancreatic secretions after stimulation with secretin for the diagnosis of chronic pancreatitis has not been adequately studied. The aim of this study was to evaluate the accuracy of the first 15-minute duodenal collection obtained during a standard 60-minute secretin stimulation test for the diagnosis of chronic pancreatitis in a large patient population. The gold standard used for the diagnosis of chronic pancreatitis was the final result of the complete 60-minute secretin stimulation test.

METHODS

The secretin stimulation test was done by placement of a Dreiling tube orally to the second portion of the duodenum. Fluoroscopy was used to guide the tube into position. The Dreiling tube has ports for simultaneous aspiration of gastric and duodenal contents. To decrease dilution of pancreatic secretions, 15 minutes of continuous aspiration of duodenal contents was performed before intravenous biologic porcine secretin administration at a dose of 1 U/kg. Immediately following secretin bolus, duodenal juice was collected by continuous aspiration in 15-minute aliquots for total of 60 minutes. The 4 samples (15, 30, 45, and 60 minute) were analyzed for bicarbonate concentration. The highest concentration of bicarbonate among the 4 aliquots was reported as peak bicarbonate concentration. Peak HCO_3^- <80 mEq/L is diagnostic of chronic pancreatitis in our laboratory.

We retrospectively reviewed 633 secretin stimulation tests performed at the University of Florida. All secretin stimulation tests were done in patients with clinical suspicion of chronic pancreatitis based on clinical presentation as well as laboratory and radiologic tests. The data extracted were the patient age and gender, HCO_3^- concentration during the first 15-minute collection, and the peak HCO_3^- concentration for the complete 60-minute secretin stimulation test.

The sensitivity, specificity, and accuracy for the first 15-minute HCO_3^- collection and the probability of a secretin stimulation test consistent with chronic pancreatitis given a HCO_3^- <80 mEq/L during the first 15-minute collection were determined. The Student *t* test was used to compare age or gender as a predictor of congruency between the first 15-minute collection and the final result of the secretin stimulation test.

RESULTS

Of the 633 patients, 490 subjects had HCO_3^- <80 mEq/L during the first 15-minute collection (Table 1). Of these 490 subjects, only 220 (true positives) also had a complete secretin stimulation test consistent with chronic pancreatitis. The remaining 270 (false positives) subjects had a HCO_3^- <80 mEq/L during the first 15-minute collection and had a normal complete standard secretin test (Table 1).

Of the 633 patients 143 (true negatives) had HCO_3^- >80 mEq/L during the first 15-minute collection and normal complete secretin stimulation test (Table 1). There were no false-negative results since, by definition, if the 15 minute HCO_3^- is >80 mEq/L, the complete standard secretin test is normal (Table 1).

The sensitivity of the 15-minute HCO_3^- test is 220/220 = 100%. (By definition, if the HCO_3^- of the first 15-minute collection is ≥80 mEq/L, the standard secretin test is normal.) The specificity of the 15-minute HCO_3^- test is 143/413 = 34.62% (95% CI, 30.03%–39.21%). In our population, the probability of a standard secretin test consistent with chronic pancreatitis given a 15-minute HCO_3^- <80 mEq/L is 220/490 = 44.90% (95% CI, 40.50%–49.30%). The accuracy of the first 15-minute collection of pancreatic secretions for the diagnosis of chronic pancreatitis is 57.34% (95% CI, 53.01%–59.34%).

There was no statistically significant difference between concordant subjects or discordant subjects with respect to age or gender (Table 2). *P* values were 0.58 for age and 0.48 for gender.

DISCUSSION

Our results demonstrate that using only the first 15-minute collection period of a standard secretin test does not

TABLE 1. Peak HCO_3^- of Secretin Stimulation Test

First 15-min HCO_3^- Concentration	Peak HCO_3^- of 60-min Secretin Stimulation Test: <80 mEq/L Chronic Pancreatitis	≥80 mEq/L Normal	Total
<80 mEq/L Positive test	220 True positive	270 False positive	490
≥80 mEq/L Negative test	0 False negative*	143 True negative	143
Total	220	413	633

*If the 15-minute HCO_3^- was ≥80 mEq/L, then the peak HCO_3^- of the secretin stimulation test was ≥80 mEq/L by definition of the secretin stimulation test.

TABLE 2. Examination of the Covariates Age and Gender

	n	Age (mean ± SD)	Male	Female
Concordant*	363	48.43 ± 15.23	128	235
Discordant†	270	49.12 ± 15.5	88	182
		$p = 0.58$	$p = 0.48$	

*Concordant: Subjects with a 15-minute HCO_3 <80 mEq/L and a peak HCO_3 of secretin stimulation test <80 mEq L or subjects with 15-minute HCO_3 ≥80 mEq/L.

†Discordant: Subjects with a 15-minute HCO_3 <80 mEq/L and a peak HCO_3 of secretin stimulation test ≥80 mEq L.

accurately measure overall pancreatic function or diagnose chronic pancreatitis. Our findings further support the data that the maximal effect of secretin on bicarbonate concentration may not occur for 30–60 minutes after injection.[8,10] In a recent study, Conwell et al[6] used endoscopic intraduodenal collection of pancreatic secretions in sedated patients to evaluate pancreatic function in patients with chronic abdominal pain. The first 15-minute duodenal collection appeared to distinguish between patients with advanced chronic pancreatitis and patients with chronic abdominal pain and negative or equivocal studies (computed tomography, ERCP, and endoscopic ultrasound). The 15-minute collection was unable to distinguish between patients with chronic abdominal pain and risk factor for chronic pancreatitis (presumably patients with early "small duct" pancreatitis) and those with pain and no risk factors (presumably patients with no pancreatitis). Those are exactly the type of patient that might be distinguishable with the secretin stimulation test done for 60 minutes. Not surprisingly, in concordance with our data, the endoscopy-based secretin test was able to distinguish the latter 2 groups at 30 ($p = 0.028$) and 60 ($p = 0.036$) minutes. The authors speculate that a single aspiration between 30 and 60 minutes after secretin injection appears to be an effective screening test for patients with chronic abdominal pain when the diagnosis of early chronic pancreatitis is suspected. It still remains unclear whether sedation given during endoscopy can interfere with the secretin stimulation test. Early studies suggest that indeed opiates have inhibitory effect on pancreatic exocrine secretion.[4] Furthermore, narcotics can increase the pressures of the sphincter of Oddi and cause relative obstruction of the flow of pancreatic juice. The so-called intraductal secretin test is an attempt to improve on the standard way of collecting pancreatic secretions via duodenal tube. Pure pancreatic juice is obtained at the time of ERCP via cannulation of the main pancreatic duct for 15 minutes after secretin injection.[5,11–14] Normal subjects in studies of pure pancreatic juice have averaged peak bicarbonate concentrations of 120–130 mEq/L. Bicarbonate concentrations in pure pancreatic juice, therefore, are typically 20%–30% higher than seen with the standard secretin test. The cut-off points (a value below which chronic pancreatitis is present) of the standard and intraductal secretin are therefore different. In the intraductal secretin test, values of 95–110 mEq/L have been proposed and are commonly used, as opposed to the cut-off of 80 mEq/L in the standard secretin test. In fact, some investigators have proposed that peak bicarbonate concentration is not the most accurate measurement in the intraductal secretin test and that either volume output or bicarbonate output (volume X concentration) are preferable.[7,11,15] Whether the intraductal secretin test in its present or modified form will prove useful for diagnosing chronic pancreatitis still remains uncertain. Our data suggest that the short 15-minute collection time used in the intraductal secretin test is inadequate to evaluate pancreatic function. A prospective comparison of the intraductal secretin test and the standard secretin test in normal controls and patients with both small duct and large duct chronic pancreatitis is needed.

The diagnosis of chronic pancreatitis remains one of the greatest challenges in gastroenterology. One has only to look at standard textbooks to note the variety of diagnostic tests available, the clear implication being that no one test is sufficient to make the diagnosis in all patients with chronic pancreatitis. Clearly, the greatest need is for a simple and accurate test to diagnose chronic pancreatitis when other tests are normal (so-called small duct chronic pancreatitis). This diagnosis is currently possible only with standard 60-minute hormonal stimulation test. Whichever technique is used to collect pancreatic secretions after stimulation with secretin to diagnose chronic pancreatitis, it is important to appreciate that the bicarbonate concentration may take up to 60 minutes to reach its peak. Our findings show that 15-minute collection of duodenal secretion after injection with secretin is an inadequate method to diagnose chronic pancreatitis.

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