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Point-of-Care Tests for Pancreatitis

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Key Messages

- Horizon scan reports provide brief summaries of information regarding new and emerging health technologies, which are identified through the CADTH Horizon Scanning Service as topics of potential interest to health care decision-makers in Canada.
- The Actim Pancreatitis test is a rapid point-of-care test that detects acute pancreatitis (including endoscopic retrograde cholangiopancreatography–related pancreatitis). It has the potential to provide a diagnosis of pancreatitis more quickly and with fewer financial and human resources. It may be particularly useful in settings that do not have quick access to laboratory services.

Actim Pancreatitis Screens for Acute Pancreatitis on the Spot

As an alternative to traditional blood tests that measure serum lipase and serum amylase, Actim Pancreatitis is a point-of-care trypsinogen-2 dipstick test that aims to diagnose or rule out acute pancreatitis in 5 minutes.

How It Works

Acute pancreatitis is a disease characterized by acute inflammation of the pancreas and destruction of the acinar cells (functional units of the pancreas).[1] Trypsinogen-2, a pancreatic enzyme, is excreted from acinar cells into the urine from early onset of acute pancreatitis.[2] Trypsinogen-2 is present in low concentration in the urine of people without pancreatitis.[3] In people with acute pancreatitis, urinary trypsinogen-2 levels are elevated in the early stages of disease and remain elevated for several days or even weeks.[4]

Actim Pancreatitis works by detecting trypsinogen-2 in urine.[4] The rapid test is carried out by dipping a test strip into a sample of freshly passed urine until it absorbs the liquid. Then, the dipstick is removed from the sample and placed horizontally. A positive result can be read as soon as it becomes visible. Two blue lines (the test line and the control line) indicate that symptoms may be due to acute pancreatitis and more investigation is needed. The test is considered negative if only 1 clear blue line is detected at 5 minutes. The control line is used to indicate proper functioning of the strip. The detection limit of the test is approximately 50 mcg/L, and the results remain positive to at least 10,000 mcg/L.[4]

Who Might Benefit?

Although the majority of acute pancreatitis cases are mild, approximately 20% can be very severe and life-threatening and potentially lead to failure of the heart, lungs, and kidneys.[5-7] The incidence of pancreatitis has been increasing worldwide.[8] In 2019, there were 29,038 new cases of pancreatitis in Canada. In the same year, there were 546 deaths and more than

2,013 years lost to disability due to pancreatitis in Canada.[9] Some people are at increased risk of acute pancreatitis, including people who are aged between 40 and 70 years, are living with obesity, are heavy consumers of alcohol, who smoke, are male, and/or have a family history of pancreatitis.[7,10,11]

Most patients with acute pancreatitis present with acute onset of severe upper abdominal pain.[12] However, there are many other causes of acute abdominal pain, including peptic ulcer, functional dyspepsia, gallstones, gastric cancer, pancreatic cancer, and abdominal aortic aneurysm. Therefore, it is essential to diagnose whether the abdominal pain is due to acute pancreatitis to initiate the appropriate treatment or to proceed to another diagnosis.[5]

Acute pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP), and occurs after approximately 5% to 10% of ERCP procedures.[13-15] ERCP is a test to examine and diagnose conditions of the liver, bile ducts, pancreas, or gallbladder.[10] In Canada, ERCP is recommended for patients with acute gallstone pancreatitis associated with bile duct obstruction or cholangitis.[16] Post-ERCP pancreatitis is fatal in 0.7% of cases.[13] Patients at high risk of post-ERCP pancreatitis include those who have a suspected sphincter of Oddi dysfunction, are younger than 50 years, are female, and/or have had more than 2 episodes of pancreatitis.[13,17] Actim Pancreatitis can also be used to detect post-ERCP acute pancreatitis.[4]

Availability in Canada

Actim Pancreatitis is not currently authorized for use in Canada or the US. According to the manufacturer,[4] the test is currently used in 42 countries around the world.

What Does It Cost?

Actim Pancreatitis is not currently available for use in Canada, so the Canadian price is unavailable. According to the UK National Institute of Health and Care Excellence,[10] the cost of Actim Pancreatitis was £4.50 in 2020. The Actim Pancreatitis test kit contains all the necessary materials needed to perform the test and can be stored at room temperature. No additional resources, sample processing, or laboratory facilities are required.[4]

Based on extrapolation of US data, pancreatitis could incur direct annual health care costs of approximately $200 million in Canada.[11]

Because Actim Pancreatis can detect acute pancreatitis immediately at an early stage, the manufacturer suggests that patients can be treated more efficiently and avoid unnecessary treatments, CT scans, and expenses.[4,18] Point-of-care testing may also reduce lengths of stay in the emergency department.[19] An observational study conducted in India[20] reported that the average time from testing to diagnosing acute pancreatitis was 29 minutes with the Actim Pancreatitis test. This was considerably shorter than the average times of 178 minutes for serum amylase and lipase testing, 242 minutes for ultrasonography, and 370 minutes for contrast-enhanced CT scan.[20]

Although several studies have reported the cost-effectiveness of point-of care tests,[21] no economic evaluations of Actim Pancreatitis have been conducted.

Current Practice

In Canada, the diagnosis of acute pancreatitis is determined by medical history and symptoms; specifically, abdominal pain and raised pancreatic enzymes in blood based on the test results of serum lipase or amylase.[6] Practice guidelines by the Best Practice in General Surgery group at the University of Toronto[16] recommend that a serum lipase test be performed in all patients with a suspected diagnosis of acute pancreatitis. The diagnosis of acute pancreatitis is based on the 2012 Atlanta Classification of Acute Pancreatitis,[22] which requires 2 of following 3 criteria:

- abdominal pain (acute onset of a persistent, severe, epigastric pain often radiating to the back)
- serum lipase activity (or amylase) at least 3 times greater than the upper limit of normal
- characteristic findings of acute pancreatitis on CT or MRI.[16]

None of the previously mentioned criteria are very reliable in diagnosing acute pancreatitis in the early stage.[3] Serum lipase increases within 4 to 8 hours of the start of symptoms, peaks at 24 hours, and returns to normal levels within 8 to 14 days. Serum amylase increases within 6 to 12 hours of the onset of acute pancreatitis and typically returns to normal within 3 to 5 days.[23] These tests are also nonspecific because other conditions can also increase the levels of lipase or amylase,[24] including peptic ulcers, salivary adenitis, inflammatory bowel disease, intestinal obstruction, peritonitis, and acute kidney injury.[25]

Contrast-enhanced CT scan is the most accurate method for diagnosing acute pancreatitis.[24,26] However, this modality is limited for routine screening due to its high costs, wait time for results, limited availability, exposure to ionizing radiation, and other potential adverse events.[3,27]

What Is the Evidence?

As demonstrated in several systematic reviews[5,10,28,29] and numerous observational studies,[3,20,23,30-34] the Actim Pancreatitis test appears to be adequately sensitive and specific for the diagnosis of acute pancreatitis in patients presenting to the hospital with abdominal pain. A summary of diagnostic test accuracy for acute pancreatitis is provided in Table 1.

All diagnostic test accuracy studies took place in hospital emergency departments and included adult patients presenting with acute abdominal pain (suspected of acute pancreatitis). The diagnosis of acute pancreatitis was based on standard criteria (acute abdominal pain, elevated levels of serum amylase and lipase, imaging results). The countries of data collection included China,[29] Egypt,[32] Finland,[10,28,29] India,[3,20,23,28-31] Italy,[29] Japan,[10,28,29,34] Spain,[28,29] Sweden,[29,32] Taiwan,[10,28] Turkey,[28,29] and the US.[29]

Some of these studies calculated and compared the diagnostic test accuracy of Actim Pancreatitis with serum amylase and serum lipase tests. Most primary studies[3,30,32,33] reported better diagnostic accuracy with Actim Pancreatitis compared with both traditional tests. Other studies[20,23,31] reported that Actim Pancreatitis was better at correctly diagnosing those with acute pancreatitis but worse at identifying those who did not have acute pancreatitis compared with serum amylase and serum lipase testing. Two systematic reviews[5,29] concluded that Actim Pancreatitis was comparable to serum amylase testing. Compared with the serum lipase test, 1 systematic review reported that Actim Pancreatitis was similar[5] and another systematic review concluded that it was inferior.[29] Because serum amylase and/or lipase were included in the reference standard to determine the diagnosis of acute pancreatitis, their diagnostic values might be overestimated due to incorporation bias, which is not the case with Actim Pancreatitis.[10,29]

One systematic review[29] and 2 prospective observational studies[14,18] assessed the reliability of Actim Pancreatitis to diagnose post-ECRP pancreatitis. Each study concluded that Actim Pancreatitis was an accurate screening test for ruling out post-ECR pancreatitis. While 1 study reported low sensitivity,[18] the systematic review reported high sensitivity.[29] The other primary study[14] found that Actim Pancreatitis correctly diagnosed all participants who had acute pancreatitis 24 hours after the procedure but was less accurate at 4 hours (60%). A summary of diagnostic test accuracy for post-ECRP pancreatitis is provided in Table 2. The diagnostic test accuracy of Actim Pancreatitis for diagnosing post-ECRP pancreatitis was comparable with or better than serum amylase, urine amylase and serum lipase testing.[18,35,36]

Table 1: Evaluation of Actim Pancreatitis for the Diagnosis of Acute Pancreatitis in Patients With Abdominal Pain

First author, year, country	Study design	Number of studies or participants	Overall sensitivity[a] (95% CI)	Overall specificity[b] (95% CI)
Systematic reviews				
Muniraj (2018)[28] US	SR and MA	17 studies[c] 2,942 participants	84% (71% to 91%)	92% (89% to 94%)
Rompianesi (2017)[5] Italy	SR and MA	5 studies 841 participants	0.72 (0.56 to 0.84)	0.90 (0.85 to 0.93)
Jin (2013)[29] China	SR and MA	14 studies 2,659 participants	0.80 (0.77 to 0.82)	0.92 (0.91 to 0.94)
Chang (2012)[24] China	SR and MA	13 studies 2,342 participants	82.3% (79.3% to 85.1%)	93.5% (92.2% to 94.6%)
Primary studies				
Chowdary (2022)[33] India	Observational	96 participants	80% (NR)	92.3% (NR)
Patel (2022)[23] India	Cross-sectional	166 participants	90.7% (NR)	87.5% (NR)
Sethy (2022)[3] India	Prospective observational	98 participants	91.5% (NR)	94.1%(NR)

First author, year, country	Study design	Number of studies or participants	Overall sensitivity[a] (95% CI)	Overall specificity[b] (95% CI)
Balineni (2021)[30] India	Cohort	100 participants	96% (NR)	100% (NR)
Simha (2021)[25] India	Prospective observational	187 participants	67.8% (57.1% to 77.25%)	90.7% (80.9% to 94.4%)
Raja (2019)[20] India	Prospective observational	134 participants	97.1% (89.8% to 99.6%)	92.4% (83.2% to 97.5%)
Mishra (2019)[31] India	Prospective observational	205 participants	93% (NR)	92% (NR)
Yasuda (2019)[34] Japan	Prospective observational	94 participants	73.1% (62% to 82%)	62.5% (39% to 82%)
El-Sheikh (2018)[32] Egypt	Observational	68 participants	100% (NR)	100% (NR)

CI = confidence interval; MA = meta-analysis; NR = not reported; SR = systematic review.

[a]Sensitivity is the test's ability to correctly diagnose participants with acute pancreatitis.

[b]Specificity is the test's ability to correctly identify participants without acute pancreatitis.

[c]Included 4 studies on post-ECRP pancreatitis.

Table 2: Evaluation of Actim Pancreatitis for the Diagnosis of Post-ECRP Pancreatitis

First author, year, country	Study design	Timing of test post-ECRP	Number of studies or participants	Overall sensitivity[a] (95% CI)	Overall specificity[b] (95% CI)
Systematic reviews					
Jin (2013)[29] China	SR and MA	1 to 6 hours	3 studies 285 participants	86% (67% to 96%)	94% (91% to 97%)
Primary studies					
Yewale (2022)[18] India	Prospective observational	4 hours	79 participants	66.7% (9.4% to 99.7%)	92.1% (83.6% to 97.1%)
Rainio (2021)[14] Finland	Prospective observational	4 hours 24 hours	388 participants 271 participants	60% (35% to 80%) 100% (70% to 100%)	99% (97% to 99%) 98% (96% to 99%)

CI = confidence interval; ECRP = endoscopic retrograde cholangiopancreatography.

[a]Sensitivity is the test's ability to correctly diagnose participants with acute pancreatitis.

[b]Specificity is the test's ability to correctly identify participants without acute pancreatitis.

Safety

No evidence was identified regarding safety issues related to the use of Actim Pancreatitis.

Issues to Consider

Although all diagnostic test accuracy studies on Actim Pancreatitis took place in hospital emergency departments, the test can potentially be performed in any clinical setting, including primary care.[10]

Several studies have reported high levels of patient satisfaction with point-of-care tests.[21] However, patient experiences with Actim Pancreatitis have not been documented.

Related Developments

Many of the diagnostic test accuracy studies of Actim Pancreatitis have been limited by small sample sizes. A clinical trial with an estimated enrolment of 1,825 participants is currently underway in the state of Indiana to assess the diagnostic accuracy of Actim Pancreatitis for the diagnosis of post-ECRP pancreatitis.[37]

Actim Pancreatitis was not developed to differentiate between severe and mild forms of acute pancreatitis. However, some studies have evaluated the accuracy of the test for predicting the severity of acute pancreatitis.[38] Its ability to detect true cases of acute pancreatitis ranged from 66% to 68% and its ability to correctly rule out acute pancreatitis was 66% to 86%.[38] Others argue that Actim Pancreatitis cannot be used to assess the severity of pancreatitis because it is not a quantitative measurement,[39] and a positive test result would still require a CT scan to confirm diagnosis, assess severity, and occurrence of complications.

Acute pancreatitis may also occur following upper abdominal surgery, such as pancreatic resection or pancreaticoduodenectomy.[40] Although it is not intended to identify these cases of pancreatitis, there is evidence that Actim Pancreatitis can identify 100% of true cases of acute pancreatitis and correctly rule out acute pancreatitis in 91% of cases after pancreatic resection. Actim Pancreatitis was also not developed to detect postoperative complications. However, the test results are significantly related with postoperative pancreatic fistula following pancreatic surgery.[41-43] However, Actim Pancreatitis failed to statistically predict postoperative pancreatic hemorrhage, delayed gastric emptying, postoperative pancreatic hemorrhage, or wound infection.[42]

Trypsinogen activation peptide (TAP) is the amino-terminus peptide released by the activation of trypsinogen.[34] The concentration of TAP correlates with the severity of acute pancreatitis.[34] TAP can be measured in urine and serum using an enzyme-linked immunosorbent assay (ELISA) kit which requires laboratory testing. A systematic review and meta-analysis[44] found that the sensitivity of urinary TAP levels to predict severity of acute pancreatitis was 71% and its specificity was 75%. The TAP ELISA test kits are expensive[45] (approximately $1,300)[46] and thus prohibitive for regular use in clinical practice.

Looking Ahead

Actim Pancreatitis is currently being used in more than 40 countries. Although it is unclear when this specific technology may be available in Canada, it could have the potential to change the way acute pancreatitis is investigated in hospital emergency departments. This simple, noninvasive test could provide rapid results without the need for blood draws or laboratory facilities. Actim Pancreatitis may be especially useful in remote or rural settings where resources are often limited and, in some cases, samples must be sent to offsite laboratories for processing. As evidence develops, modification of the cut-off point may potentially increase the test's accuracy for predicting the severity of acute pancreatitis.

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