

## CHOOSING WISELY®: THINGS WE DO FOR NO REASON

## Amylase Testing for Abdominal Pain and Suspected Acute Pancreatitis

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The “Things We Do for No Reason” (TWDFNR) series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent “black and white” conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

A 37-year-old man presents to the emergency department complaining of acute onset abdominal pain associated with nausea and vomiting. The pain is constant and achy in nature. It is located in the upper abdomen and radiates to the back. The patient reports binge alcohol consumption the day prior to the onset of his pain.

His physical examination is remarkable for fever, with a temperature of 100.6°F and epigastric tenderness to palpation without rebound or guarding. He is not hypotensive, and there is no evidence of the Cullen sign or Grey-Turner sign.

In this patient presenting with acute abdominal pain, is ordering amylase alone, lipase alone, or amylase and lipase together the most high-value method to evaluate him for acute pancreatitis?

### WHY YOU MIGHT THINK AMYLASE TESTING IS HELPFUL

Amylase was one of the earliest, easily measurable laboratory tests that provided a relatively high degree of sensitivity and specificity for identifying patients with acute pancreatitis among those presenting with acute abdominal pain.<sup>1</sup> Since the introduction of amylase, additional tests, including lipase, have been introduced into clinical practice, which offer superior sensitivity and specificity compared to amylase for the diagnosis of acute pancreatitis.<sup>2</sup> However, amylase testing is routinely ordered at many healthcare institutions, with co-ordering of these tests occurring greater than 90% of the time in some cases.<sup>3,4</sup> Amylase testing may remain in clinical practice for several reasons

including: (1) greater experience with amylase given its earlier introduction into clinical practice, (2) the belief that co-ordering amylase and lipase provides greater accuracy than either test alone, (3) the notion that pancreatic enzymes provide prognostic information or allow monitoring of clinical progress, and (4) coupling of amylase and lipase in electronic order sets or including the tests together as part of routine lab panels used for the evaluation of abdominal pain.

### WHY AMYLASE TESTING OFFERS NO ADDITIONAL VALUE TO LIPASE TESTING

#### Is Amylase More Accurate Than Lipase in the Diagnosis of Acute Pancreatitis?

In a number of studies, lipase has generally been found to be both more sensitive and more specific than amylase for the diagnosis of acute pancreatitis.<sup>5-9</sup> A large study by Smith and colleagues, which included 8937 patients who were initially evaluated in the emergency department, found that lipase had a superior area under the receiver operating curve when compared to amylase (0.948 vs 0.906). At a diagnostic threshold of 208 U/L for lipase and 114 U/L for amylase, the authors found that lipase compared to amylase had a superior sensitivity (90.3% vs 78.7%), specificity (93.0% vs 92.6%), positive likelihood ratio (14.1 vs 10.6), and a similar negative likelihood ratio (0.1 vs 0.1).<sup>5</sup>

The observed superiority of lipase over amylase may be related to a number of underlying factors. For instance, amylase measurements often include  $\alpha$ -amylase from the salivary glands and various macroamylase molecules that may not be related to pancreatic injury, whereas lipase measurements are more specific to the pancreas itself.<sup>5</sup> As a result, amylase can be elevated in a number of conditions that are unrelated to acute pancreatitis including parotitis, macroamylasemia, and some cancers.<sup>10</sup> In addition, because lipase remains elevated longer than amylase, it may be more accurate in the setting of delayed presentations of acute pancreatitis.

#### Does Amylase Co-Ordered With Lipase Increase Diagnostic Accuracy?

Multiple studies have explored whether amylase provides additional diagnostic information when co-ordered with lipase. A study by Chase et al. found that amylase and lipase were closely correlated, making them likely redundant measures.<sup>7</sup> Viel and colleagues developed a logistic regression model exploring the value of various parameters in the

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diagnosis of acute pancreatitis. Although they found that lipase and amylase were both accurate in univariate analyses, a multivariate analysis found that the addition of amylase did not improve the model when compared to lipase alone.<sup>9</sup> In a more recent study by Treacy et al., the investigators explored the accuracy of amylase and lipase in the diagnosis of acute pancreatitis, either alone or in combination, at days 1, 2, and 3 following presentation. In addition to showing that lipase was more accurate than amylase, their results also demonstrated that amylase in addition to lipase did not provide additional diagnostic accuracy compared to lipase alone, as assessed by partial area under the receiver operating curve (0.125 vs 0.128 at day 1, 0.050 vs 0.054 at day 3).<sup>6</sup> Finally, although some early reports suggested that the lipase to amylase ratio could be helpful to distinguish alcoholic pancreatitis from nonalcoholic pancreatitis, later studies have not confirmed these results.<sup>11,12</sup>

### Does Either Amylase or Lipase Add Prognostic Information?

Although both amylase and lipase are useful in the diagnosis of pancreatitis, neither correlates well with severity of illness or clinical resolution of pancreatitis.<sup>10</sup> As a result, the level of elevation of pancreatic enzymes is not included in the major tools used to assess severity of illness, including Ranson's criteria,<sup>13</sup> APACHE II (Acute Physiology and Chronic Health Evaluation II), or the computed tomography (CT) severity index.<sup>14</sup> Newer scoring systems, including the Bedside Index of Severity in Acute Pancreatitis<sup>15</sup> and the Harmless Acute Pancreatitis Score<sup>16</sup> also do not include pancreatic enzymes in their algorithms.

### What Do Guidelines and Thought Leaders Say About Using Amylase?

The 2006 Practice Guidelines in Acute Pancreatitis state that it is not necessary to order amylase and lipase together under normal circumstances, and also note that serum lipase is the preferred diagnostic study. In addition, these guidelines state that daily measurement of pancreatic enzymes after the initial diagnosis "has limited value in assessing the clinical progress of the illness or ultimate prognosis."<sup>10</sup> The 2013 American College of Gastroenterology guidelines provide stronger support for ordering lipase alone, stating "serum amylase alone cannot be used reliably" and that "serum lipase is preferred."<sup>2</sup>

International guidelines also support the use of lipase alone for the diagnosis of acute pancreatitis. The UK guidelines for the management of acute pancreatitis offer their strongest recommendation supporting the use of lipase alone rather than amylase, unless lipase testing is not available.<sup>17</sup> The Japanese guidelines state the "lipase level is the best pancreatic enzyme parameter" and additionally do not support the co-ordering of amylase and lipase together.<sup>18</sup>

Finally, a group of experts in pathology and laboratory medicine at major academic medical centers have identified serum amylase as one of the top 10 antiquated tests within the clinical pathology laboratory.<sup>19</sup>

### WHAT YOU SHOULD DO INSTEAD: ORDER LIPASE ALONE

In all cases where a patient presents with abdominal pain concerning for acute pancreatitis, we recommend ordering lipase alone rather than either amylase alone or co-ordering amylase and lipase. In addition, we suggest that healthcare providers do not perform daily measurement of pancreatic enzymes.

When lipase testing is available, amylase testing provides no clinical value in assisting with the diagnosis or management of acute pancreatitis, but comes at a significant cost to patients. At an average charge of \$35 per test, amylase testing represents at least \$19 million in annual charges to Medicare alone, according to 2013 payment data.<sup>20</sup> Given that the average charge for a lipase test is \$41, it is also difficult to argue that amylase testing is significantly less costly than lipase testing. In addition to the direct costs, amylase tests in these settings can result in diagnostic delays or misdiagnosis, imposing additional costs on patients and the health system. For instance, a patient who presents with symptoms of pancreatitis, a positive lipase, and a negative amylase could receive an unnecessary CT scan to further assess for acute pancreatitis, despite already meeting diagnostic criteria based on the symptoms and lipase test alone.

At institutions where amylase and lipase are listed together in common order sets, removing amylase from these order sets may be a simple, durable intervention to reduce amylase testing.<sup>3</sup> Educational interventions aimed at alleviating some of the cognitive factors associated with amylase and lipase co-ordering described above should also be considered.

### RECOMMENDATIONS

1. In patients suspected of having acute pancreatitis, lipase should be ordered alone rather than ordering either amylase alone or amylase and lipase together.
2. Pancreatic enzymes should not be repeated after making the diagnosis of acute pancreatitis, as this practice does not provide additional information that is of clinical utility.

### CONCLUSION

In the evaluation of acute pancreatitis, the majority of the evidence suggests that amylase, when compared to lipase, has inferior sensitivity and specificity, adds no additional diagnostic information when co-ordered, and does not provide additional prognostic information (Table 1). In this setting, many guidelines and thought leaders recommend ordering lipase alone

**TABLE 1. Test Characteristics of Amylase and Lipase**

Test Characteristic	Amylase	Lipase
Sensitivity <sup>3</sup>	78.7%	90.3%
Specificity <sup>3</sup>	92.6%	93.0%
Useful when presentation of pancreatitis is delayed	Sometimes	Almost always
Useful to assess severity	No	No
Useful to assess clinical resolution	No	No
Peak	12–72 hours	24 hours
Return to normal	3–5 days	8–14 days

rather than either amylase alone or co-ordering amylase and lipase. In addition, daily monitoring of pancreatic enzymes is not recommended because it does not help assess clinical progress or severity of illness. As a result, we believe that amylase testing should no longer be ordered for patients with suspected acute pancreatitis. Ordering amylase for the evaluation of abdominal pain is a “thing we do for no reason.”

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*Do you think this is a low-value practice? Is this truly a “Thing We Do for No Reason?” Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWFNDR) and liking it on Facebook. We invite you to propose ideas for other “Things We Do for No Reason” topics by emailing TWFNDR@hospitalmedicine.org.*

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