FPIN's Clinical Inquiries

A1C Testing in the Diagnosis of Diabetes Mellitus

Clinical Question

Can A1C measurements be used to diagnose diabetes mellitus?

Evidence-Based Answer

A1C testing is highly specific compared with a two-hour oral glucose tolerance test (OGTT) or a fasting plasma glucose test. However, because A1C testing is not sensitive enough to rule out diabetes if levels are normal, the test should not be used for diagnosing diabetes.1 (Strength of recommendation: C).

Evidence Summary

The accuracy of A1C testing for the diagnosis of diabetes was first evaluated using pre-1997 World Health Organization (WHO) criteria for a diabetes diagnosis (i.e., OGTT result more than 140 mg per dL [7.8 mmol per L] fasting or more than 200 mg per dL [11.1 mmol per L] at two hours). A meta-analysis1 (including 10 studies that evaluated A1C levels of 8,984 patients) that used a cutoff (i.e., upper limit of normal) A1C level of 6.3 percent (two standard deviations [SD] above the mean) showed that A1C testing was 66 percent sensitive and 98 percent specific for diagnosing diabetes (Table 1). Based on an assumed diabetes prevalence rate of 6 percent in the general population (i.e., persons without known diabetes), 63 percent of patients with an A1C level more than 6.3 percent would have diabetes (positive predictive value [PPV] = 63 percent).

<table>
<thead>
<tr>
<th>Accuracy of A1C Testing for Diabetes</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutoff A1C level (SD) above mean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peters, et al., 19961</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.3 (2)</td>
<td>66</td>
<td>98</td>
<td>63</td>
</tr>
<tr>
<td>6.8 (3)</td>
<td>48</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>7.3 (4)</td>
<td>36</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>Rohlfing, et al., 20002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.6 (1)</td>
<td>83.4</td>
<td>84.4</td>
<td>25</td>
</tr>
<tr>
<td>6.1 (2)</td>
<td>63.2</td>
<td>97.4</td>
<td>57</td>
</tr>
</tbody>
</table>
Positive predictive values were calculated using an assumed diabetes prevalence rate of 6 percent in the general population (i.e., persons without known diabetes).

Information from references 1 and 2.

A subsequent study\(^2\) that used current WHO criteria for defining diabetes (i.e., fasting plasma glucose of 126 mg per dL [7.0 mmol per L] or more) showed similar results. This cross-sectional study\(^3\) of 6,559 patients that used a cutoff A1C level of 6.1 percent and assumed a diabetes prevalence rate of 6 percent showed A1C testing was 63.2 percent sensitive and 97.4 percent specific for diagnosing diabetes (PPV = 57 percent). A subgroup analysis\(^2\) of these results showed that the sensitivity of A1C testing was considerably higher in Mexican Americans and blacks (83.6 and 75.8 percent, respectively) compared with non-Hispanic whites (58.6 percent). The reason for these differences is unclear; however, these results may suggest physiologic variations among ethnic groups. If this is verified in future, larger studies, A1C testing may have a role in diagnosing diabetes in some patient populations.

Recommendations from Others

The American Diabetes Association (ADA) does not recommend A1C testing for the diagnosis of diabetes.\(^3\) Instead, it recommends fasting plasma glucose testing (126 mg per dL or more is diagnostic) as the test of choice because it is easier and faster to perform and less expensive than other screening tests. Table 2 includes the ADA criteria for diagnosing diabetes. Although the ADA guideline points out that A1C testing historically had not been standardized among laboratories, the test has become widely standardized in the United States since the guideline's publication.\(^4\) The European Diabetes Policy Group guideline\(^5\) also does not recommend A1C testing for diagnosing diabetes and recommends confirming the diagnosis in persons with elevated A1C levels using fasting plasma glucose testing (126 mg per dL or more is diagnostic).

**Table 2**

**American Diabetes Association Criteria for the Diagnosis of Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose</td>
<td>≥ 126 mg per dL (7.0 mmol per L)</td>
</tr>
<tr>
<td>Two-hour postload glucose</td>
<td>≥ 200 mg per dL according to an oral glucose tolerance test</td>
</tr>
</tbody>
</table>

*In the absence of unequivocal hyperglycemia, these criteria should be confirmed by
repeat testing on another day.

†-A casual glucose measurement is determined any time of day without regard to
time since last meal.

‡-Fasting is defined as no caloric intake for at least eight hours.

§-Oral glucose tolerance tests are not recommended for routine clinical use and
should be performed as described by the World Health Organization (i.e., using a
glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in
water).

Adapted with permission from Report of the Expert Committee on the Diagnosis and

Clinical Commentary

Although most of the literature on diabetes includes the two-hour OGTT as the standard test for
diagnosing diabetes, in daily clinical practice, this approach is not always feasible. Fasting
plasma glucose testing has been shown to have slightly lower sensitivity for predicting
microvascular complications from diabetes compared with the two-hour OGTT, but it is easier to
perform compared with the two-hour OGTT. Therefore, fasting plasma glucose testing is widely
used as the preferred diagnostic test.

Some physicians believe that because glycemic treatment for diabetes is not aggressively
initiated until A1C levels are 7 percent or more, A1C testing can be used for diagnosis despite its
low sensitivity. However, there are other important interventions (e.g., improving blood pressure,
lowering low-density lipoprotein cholesterol, aspirin therapy, influenza vaccination) that are
recommended for patients with diabetes, even those with A1C levels less than 7 percent. Therefore, fasting plasma glucose testing remains the preferred diagnostic test for diabetes.

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Author disclosure: Nothing to disclose.
REFERENCES


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