The Prediabetes Debate: Should the Diabetes Diagnostic Threshold Be Lowered, Allowing Clinicians to Intervene Earlier?

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I believe that the diagnosis of type 2 diabetes mellitus (T2DM) should be broadened to match the glycemic thresholds currently used for prediabetes. This would eliminate the need for a separate category, the "prediabetes" nomenclature, and allow for earlier therapeutic intervention in patients. Current diabetes diagnostic thresholds do not reflect the latest advancements in T2DM understanding. The latest in T2DM research suggests that intervening and treating prediabetes earlier could potentially offer better clinical outcomes and enhance patients' quality of life, as cell and tissue damage occurs early and leads to dysfunction prior to a diabetes diagnosis.[1] T2DM is a highly complex disease with multifactorial causes beyond hyperglycemia that should be considered, such as hyperlipidemia, insulin resistance, hyperinsulinemia, and autoimmune inflammatory mechanisms that lead to β-cell dysfunction or failure, which results in hyperglycemia.

Prediabetes is associated with micro- and macrovascular complications that can occur early in the progression to frank disease state.[1,2] This phase of diabetes also includes insulin resistance, impaired incretin action, insulin hypersecretion, increased lipolysis, and ectopic lipid storage—all of which damage β cells. These dysfunctions are also present in the frank diabetic disease state.[3,4] Furthermore, diabetic retinopathy occurs in 8% to 12% of patients with prediabetes, and retinopathy begins earlier than previously thought, with neuroinflammation occurring even before vascular damage.[5,6] Unfortunately, these neuro-inflammatory lesions cannot be detected with the typical instruments used in an ophthalmologist's office.

It is believed that, through the principle of metabolic memory, even a moderate increase or episodic spikes in blood glucose can lead to negative effects in prediabetic patients who are susceptible to T2DM.[1,5] Therefore, a lower diabetes diagnostic threshold could allow for earlier, more precise, and personalized therapies based on each patient's individual risk factors and biomarkers. With a diagnosis of T2DM at the current prediabetes threshold, patients could receive treatment covered by health

insurance while in the “prediabetic” state—treatment that would not have been previously approved. Patients should be treated earlier and on an individual basis with counseling on diet and lifestyle changes and antidiabetic agents to reduce glycemic levels, preserve β cells, and reduce cardiovascular [CV] or renal risk, among other complications.[6,7]

Moreover, the newer agents for treating diabetes such as glucagon-like pepetide-1 receptor agonists and sodium-glucose cotransporter 2 inhibitors, which are also associated with reduction in adverse CV and/or renal outcomes, could be beneficial if administered early in the prediabetic stage of disease.[8,9]

Early lifestyle and pharmacologic interventions can reduce the rate of progression from prediabetes to diabetes as well as complications and associated conditions, and even potentially result in remission or a full reversal of diabetes. These “side benefits” of lowering the diabetes diagnostic threshold (over and above glycemic control) make any cost-effectiveness calculations all the more advantageous to individual patients as well as to society.

Given the numerous benefits of earlier intervention for diabetes treatment, I believe a call to re-evaluate the current diabetes diagnostic threshold is in order, as it will do a great service for all patients who are currently at risk for developing T2DM.

References

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