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Advantages and Pitfalls of the Glycated Hemoglobin A1c Measurement in Acute Coronary Syndrome: Start Simple, Evolve to More Sophisticated

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We would like to thank Cetin et al[1] for their interest in our work titled, "Association of Prediabetes With Higher Coronary Atherosclerotic Burden Among Patients With First Diagnosed Acute Coronary Syndrome"[2] about the association of prediabetes with higher coronary atherosclerotic burden among patients with first diagnosed acute coronary syndrome (ACS). Cetin et al reported some concerns about the categorization of the study population using only glycated hemoglobin (HbA_{1c}) level might be misleading and especially overdiagnosing prediabetic population.[1]

Numerous studies have documented that hyperglycemia is frequent in patients hospitalized with ACSs. This affects patients with and without established diabetes mellitus (DM) or prediabetes and is associated with adverse outcomes.[3-6] For many patients, ACS hospitalization represents an event during which previously unrecognized DM may be diagnosed. Indeed, a large percentage of patients with DM present with a first ACS before their DM is diagnosed. Because the cardiologist often may be the first clinician to diagnose an ACS patient with DM or prediabetes, it is incumbent upon them to understand the disease process and the interventions necessary to improve outcome.[7] Most recent guidelines by the European Society of Cardiology (ESC) in collaboration with European Association for the Study of DM have recommended that all patients with ACS are screened for DM.[8]

There is currently no uniform, accepted definition for hyperglycemia in the setting of ACS. Prior studies used various blood glucose cut points, from $\geq$110 to $\geq$200 mg/dL.[3] The American Heart Association (AHA) Scientific Statement on Hyperglycemia and ACS suggest using a random glucose level $\geq$140 mg/dL observed at any time over the course of ACS hospitalization as the definition of hyperglycemia.[9] This AHA position advocates for a glucose treatment threshold of $\geq$180 mg/dL with suggested therapeutic target of glucose control specified at 140 to 180 mg/dL.[9]

Despite the recognition of the importance of diagnosing dysglycemia in patients with ACS, there remains a lack of consensus on the best screening modality. Currently, there are 2 main diagnostic criteria for dysglycemia: the World Health Organization (WHO)[10] and the American DM Association (ADA) criteria.[11] Diabetes mellitus may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-hour plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT) or HbA_{1c} criteria. Generally, FPG, 2-h PG during 75-g OGTT, and HbA_{1c} are equally appropriate for diagnostic testing.[11] The same tests may be used to screen for and diagnose DM and to detect individuals with prediabetes.[11] However, the ADA and WHO guidelines provide no consensus on how to identify metabolic derangement in high-risk groups such as patients with ACS. The ESC guidelines for the diagnosis of dysglycemia in patients with cardiovascular disease recommend a staged approach of the HbA_{1c} and FPG measurements as the first screening tests for all patients with cardiovascular disease, adding the OGTT only for those with inconclusive results.[12] However, the current screening methods using the FPG, insulin level, or the OGTT have limitations in the ACS settings.[13] The main limitation of the insulin levels is also that it is resource intensive.[14] Use of universal HbA_{1c} screening on admission appeared to be more practical and effective with improved detection rates in ACSs.[15] While the WHO approved the use of HbA_{1c} as the preferred screening test in the diagnosis and targeted

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screening for DM,[10] the National Institute of Health and Care Excellence (NICE) recommend that all patients with ACS with admission blood glucose concentrations $\geq$11.0 mmol/L should have an FPG no earlier than day 4 after ACS onset or have an HbA_{1c} test before discharge.[16] It has suggested FPG should not be measured within the first 4 days of the acute event.[16] The 2-h PG is also not helpful shortly after ACS due to adrenergic activation and insulin resistance.[17] The early OGTT is valid, but the test should not be performed earlier than 4 to 5 days after the event, especially in patients with extensive infarctions[8,18,19] since it can also be affected by multiple factors, which include carbohydrate diet and physical activity levels prior to the test as well as the severity of myocardial damage and timing of the test in relation to an index event.[19] The NICE recommend against routine use of the OGTT in patients with ACS and with FPG and HbA_{1c} in the normal range.[16] Furthermore, in the current era of early reperfusion therapies, many patients with ACS are discharged earlier and may not be screened with day 4 FPG measurement due to increasingly shorter length of stays.[20] Therefore, there are many advantages of using HbA_{1c} rather than FPG, insulin levels, or OGTT for screening and diagnosing DM in an acute setting: less sensitivity to preanalytical variables, lower within-subject biological variability, little/no diurnal variations, and little/no influence from acute stress and illness.[21]

When using HbA_{1c} to diagnose DM, it is important to recognize that HbA_{1c} is an indirect measure of average blood glucose levels and to take other factors into consideration that may impact hemoglobin glycation independent of glycemia including age, race/ethnicity, and anemia/hemoglobinopathies.[11] However, the use of a simple HbA_{1c} screening method in clinical practice can detect new-onset DM in approximately 1 in 10 patients with high-risk post ACS,[13] and the test can be performed in the nonfasting state and reflects average glucose concentration over the preceding 3 months approximately.[12] Therefore, in our opinion, HbA_{1c} may represent a screening tool for glucose intolerance from the early phase on in patients with ACS and should be measured in all patients with ACS[22] as a worthwhile, simple, and practical screening option.[13,23]

Declaration of Conflicting Interests

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