

Efficiency of glycosylated hemoglobin (HbA1c) as a predictive marker for diabetic complications

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Abstract

Glycosylated hemoglobin (HbA1c) is a key biomarker for assessing long-term glycemic control in individuals with diabetes mellitus, providing insight into average blood glucose levels over the past two to three months. This review evaluates the efficacy of HbA1c as a predictive marker for diabetic complications, which are categorized into microvascular (including retinopathy, nephropathy, and neuropathy) and macrovascular (primarily cardiovascular diseases). Extensive research demonstrates a strong correlation between elevated HbA1c levels and increased risks of complications, with landmark studies such as the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) establishing the benefits of maintaining HbA1c below 7% in reducing complications. However, the use of HbA1c is not without limitations, including interindividual variability, the inability to capture daily glucose fluctuations, and the potential for misleading results due to conditions such as hemoglobinopathies. As a result, while HbA1c remains a cornerstone in diabetes management and a valuable tool for predicting the risk of complications, a multifaceted approach that incorporates additional glucose monitoring methods is essential for optimizing patient care. This review aims to highlight both the strengths and limitations of HbA1c, as well as the need for ongoing research to enhance its predictive accuracy in clinical settings.

Introduction

Glycosylated hemoglobin (HbA1c) has become a cornerstone in the management and diagnosis of diabetes mellitus, fundamentally influencing clinical practice and patient outcomes. As an indicator of long-term glycemic control, HbA1c measures the percentage of hemoglobin molecules that are modified by glucose, reflecting the average blood glucose levels over the past two to three months. Since the discovery of this relationship, HbA1c has served as a critical metric in both clinical settings and research, facilitating effective diabetes management strategies and standardizing care across diverse populations. The American Diabetes Association (ADA) and various other health organizations have established guidelines that recommend maintaining an HbA1c level of less than 7% for most adults with diabetes, aiming to minimize the risk of complications and improve quality of life [1].

Diabetes mellitus, characterized by chronic hyperglycemia and associated with metabolic anomalies, can lead to a range of complications that adversely affect various organ systems. The complications can be broadly classified into two categories: microvascular and macrovascular. Microvascular complications include diabetic retinopathy, nephropathy, and neuropathy, which pose significant risks of vision loss, kidney failure, and impaired nerve function, respectively. Macrovascular complications primarily involve cardiovascular diseases, including heart attack and stroke, which are the leading causes of morbidity and mortality among individuals with diabetes. Given the diverse and severe implications of these complications, timely intervention and effective disease management are paramount.

The relationship between HbA1c levels and the risk of developing these complications has been the subject of extensive research. Landmark studies, such as the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS), have established that improved glycemic control, reflected by lower HbA1c levels, is associated with a significant reduction in the incidence and progression of both microvascular and macrovascular complications [2, 3]. For example, findings from the DCCT revealed that intensive glycemic control significantly reduced the risk of retinopathy by 76%, emphasizing the role of HbA1c as a critical predictor of clinical outcomes in patients with Type 1 diabetes [2].

Despite its advantages, the application of HbA1c as a predictive marker is not without challenges. The variability of individual responses to glucose levels, the influence of comorbid conditions, and the presence of hemoglobinopathies can affect HbA1c results, potentially leading to misleading interpretations [4]. Moreover, HbA1c represents an average measure, which can obscure significant fluctuations in daily glucose levels that may also impact complications. This necessitates a comprehensive approach to diabetes management, wherein HbA1c results are integrated with additional monitoring tools, such as continuous glucose monitoring systems, to provide a more nuanced understanding of a patient's glycemic status.

The growing recognition of the limitations of HbA1c has prompted researchers and clinicians to explore the development of new biomarkers and the advancement of therapeutic strategies aimed at improving glycemic control. Nonetheless, HbA1c remains a vital component of diabetes care, serving as a benchmark for treatment effectiveness and a guide for clinical decision-making. As new methods and technologies emerge, the importance of utilizing HbA1c in conjunction with an individual's overall treatment plan will be essential for optimizing patient outcomes and minimizing the risks of diabetic complications.

HbA1c is more than just a laboratory value; it is a powerful tool that informs clinical practice and shapes the management of diabetes. It provides insight into the long-term effectiveness of glycemic control strategies and serves as a guide for predicting potential complications. This review seeks to dissect the efficiency of HbA1c as a predictive marker for diabetic complications, taking into account its strengths and limitations while exploring avenues for enhancing its utility in clinical settings.

Review:

Understanding HbA1c

HbA1c results from a non-enzymatic glycation process where glucose molecules bond to hemoglobin, thereby forming glycated hemoglobin. The concentration of HbA1c is reflective of an individual's average blood glucose levels—higher glucose concentrations lead to higher HbA1c percentages. The American Diabetes Association recommends maintaining an HbA1c level of less than 7% for most adults with diabetes to mitigate the risk of complications [1]. This threshold is based on extensive clinical research demonstrating a relationship between HbA1c levels and the risk of long-term complications. Nevertheless, clinicians must recognize that HbA1c is not merely

a singular metric of glucose control; it provides a broader perspective on a patient's diabetes management, allowing for informed treatment decisions.

Strengths of HbA1c as a Predictive Marker

One of the most compelling strengths of HbA1c as a predictive marker lies in the substantial body of correlational evidence that links its levels with the onset and progression of diabetic complications. Research from the Diabetes Control and Complications Trial (DCCT) established that intensive glycemic control—as indicated by reduced HbA1c levels—significantly decreased the incidence of microvascular complications in Type 1 diabetes [2]. This landmark study underscored the critical importance of maintaining lower HbA1c levels, establishing a clear connection between better glycemic control and diminished risk of complications such as retinopathy and nephropathy. Similarly, the United Kingdom Prospective Diabetes Study (UKPDS) provided robust evidence in a large cohort of Type 2 diabetes patients, demonstrating that even a modest reduction in HbA1c could lead to meaningful decreases in the risks for both microvascular and macrovascular complications [3]. The accumulated evidence supports the use of HbA1c not only as a monitoring tool but also as a valuable predictive marker for assessing complication risks in individuals with diabetes.

In addition to its correlation with complications, HbA1c's predictive validity is illustrated by the well-documented relationship between elevated levels and increased progression of diabetic retinopathy. A major analysis conducted by Stratton et al. (2000) revealed that for every 1% increase in HbA1c, there was a corresponding 30% increase in the likelihood of developing diabetic retinopathy [4]. This finding reinforces the notion that controlling HbA1c levels is paramount in preventing one of the most severe complications associated with diabetes. Moreover, HbA1c measurements facilitate long-term monitoring, providing a stable assessment of glycemic control over time, which is crucial as daily glucose fluctuations may be misleading. Unlike daily self-monitoring of blood glucose, which reflects short-term fluctuations influenced by factors such as diet and exercise, HbA1c serves as an average over months, projecting a picture of long-term management [5].

It is also important to note the standardization of HbA1c testing, which is widely implemented across clinical practice. The American Diabetes Association and the International Federation of Clinical Chemistry and Laboratory Medicine have provided guidelines ensuring uniformity in HbA1c measurement processes, thus allowing for consistent interpretability of results [6]. Such standardization enhances the reliability of HbA1c as a marker across diverse healthcare settings and populations, further enhancing its practical utility in routine diabetes management.

Limitations of HbA1c as a Predictive Marker

Despite its significant strengths, HbA1c does present notable limitations, primarily stemming from its inherent variability and the influence of individual patient characteristics on its accuracy as a predictive marker. One considerable drawback is the substantial interindividual variability observed in the relationship between HbA1c levels and complications. Factors such as age, ethnic background, and genetic predispositions can cause disparities in HbA1c levels that do not necessarily correlate with a patient's actual glycemic status. For example, conditions like anemia or hemoglobinopathies can artificially lower or raise HbA1c levels, thereby skewing the interpretation of glycemic control and risk of complications [7]. This variability complicates the use of HbA1c as a straightforward predictive measure, as two patients with identical HbA1c levels may have vastly different underlying glucose profiles and risk factors for complication development.

Additionally, HbA1c's nature as an average measurement can lead to missed glycemic excursions—periods of hyperglycemia or hypoglycemia that may adversely impact overall health. This averaging effect can conceal acute glucose fluctuations that could contribute to complications, as patients with stable but high glucose levels may have the same HbA1c as those with significant but brief spikes in blood glucose [8]. Consequently, relying solely on HbA1c may result in an incomplete picture of a patient's glycemic control and subsequently their risk for complications. Moreover, HbA1c reflects historical glucose exposure rather than current glucose levels, which may delay clinical responses necessary to prevent acute complications [9].

Furthermore, the lack of universally accepted thresholds for HbA1c complicates its role as a predictive marker. The onset of complications may vary considerably based on multiple factors, leading to challenges in establishing a specific HbA1c benchmark that indicates impending complications. Although lowering HbA1c levels has shown protective benefits, determination of precise thresholds suitable for risk stratification remains complex and contingent on factors such as one's age, duration of diabetes, and the presence of comorbid conditions [10].

Conclusion

In summary, while HbA1c serves as a critical marker in diabetes management, highlighting its utility in predicting diabetic complications, it also possesses inherent limitations that clinicians should carefully consider. The established link between HbA1c levels and the risk of microvascular and macrovascular complications is supported by significant clinical evidence; however, individual variability and the average nature of HbA1c measurements necessitate a multifaceted approach to patient assessment. This may involve integrating HbA1c results with other biomarkers, continuous glucose monitoring, and individualized patient factors in order to optimize diabetic management and enhance patient-centered care. Further research focused on addressing these limitations and improving predictive accuracy will be essential for refining diabetes management strategies and enhancing patient outcomes in clinical practice.

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