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PERSPECTIVES

Continuous Glucose Monitoring: A Transformative Approach to the Detection of Prediabetes

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Abstract: Prediabetes, as an intermediary stage between normal glucose homeostasis and overt diabetes, affects an estimated 720 million individuals worldwide, highlighting the urgent need for proactive intervention strategies. Continuous glucose monitoring (CGM) emerges as a transformative tool, offering unprecedented insights into glycemic dynamics and facilitating tailored therapeutic interventions. This perspective scores the clinical significance of even slightly elevated fasting blood glucose levels and the critical role of early intervention. CGM technology provides real-time, continuous data on glucose concentrations, surpassing the constraints of conventional monitoring methods. Both retrospectively analyzed and real-time CGM systems offer valuable tools for glycemic management, each with unique strengths. The integration of CGM into routine care can detect early indicators of type 2 diabetes, inform the development of personalized intervention strategies, and foster patient engagement and empowerment. Despite challenges such as cost and the need for effective utilization through training and education, CGM's potential to revolutionize prediabetes management is evident. Future research should focus on refining CGM algorithms, exploring personalized intervention strategies, and leveraging wearable technology and artificial intelligence advancements to optimize glycemic control and patient well-being.

Keywords: continuous glucose monitoring, prediabetes, glycemic control, diabetes prevention strategies, transformative approach

Introduction

Prediabetes, positioned as the intermediary stage between normal glucose homeostasis and overt diabetes, is marked by blood glucose levels elevated above the normal range but not yet meeting the diagnostic criteria for diabetes.[1] This condition, currently affecting an estimated 720 million individuals worldwide, underscores the pressing need for proactive intervention strategies to mitigate its progression into full-blown diabetes and associated complications.[2] As the global burden of diabetes persists, prediabetes emerges as a critical early warning sign, compelling us to explore and implement effective management approaches.

In recent years, authoritative bodies such as the American Diabetes Association (ADA) and global consensuses have refined the diagnostic criteria for prediabetes. In 2024, the ADA defines individuals with prediabetes[3] as those with impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) and/or an A1C level of 5.7–6.4% (39–47 mmol/mol). Impaired fasting glucose is characterized by fasting plasma glucose (FPG) levels ranging from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) (78, 79), while impaired glucose tolerance is defined by 2-hour post-load glucose (2-h PG) levels of 140 to 199 mg/dL during a 75g oral glucose tolerance test (OGTT). Similarly, the Global Consensus has established comparable thresholds, emphasizing the importance of early identification and intervention to prevent the progression to diabetes.[4] In this endeavor, continuous glucose monitoring (CGM) stands as a transformative tool, offering unprecedented insights into glycemic dynamics and facilitating tailored therapeutic interventions.

The Urgency of Prediabetes Management

Recent epidemiological studies[5,6] have convincingly demonstrated the clinical significance of even slightly elevated fasting blood glucose (FPG) levels, underscoring the urgent need for timely and effective pre-diabetes management.

Individuals with FPG exceeding 5.6 mmol/L are confronted with a significantly heightened vulnerability to diabetes and cardiovascular disease, underscoring the pivotal role of early intervention in stemming this rising tide.[2,7]

Moreover, the intensification of insulin resistance at FPG levels above 4.9 mmol/L, tripling the risk of diabetes, underscores the delicate balance that must be maintained to avert disease progression.[8] The critical importance of identifying and targeting individuals within this prediabetic range, who, despite their heightened risk, may often go unrecognized and untreated. Beyond fasting glucose levels, postprandial glucose excursions, particularly the 1-hour postprandial glucose measurement, have emerged as more potent predictors of future type 2 diabetes risk compared to the traditional 2-hour postprandial assessment.[9] This discovery underscores the limitations of current monitoring practices and the urgent need for more comprehensive glucose monitoring strategies encompassing the entire spectrum of glycemic variability.

The disparity between the American Diabetes Association's prediabetes threshold of FPG ≥ 5.6 mmol/L and the global consensus diagnostic cut-off of FPG > 6.1 mmol/L highlights a gap in care for those with intermediate FPG levels.[2] This subgroup, though facing an elevated risk of diabetes, may inadvertently slip through the cracks of targeted interventions due to this inconsistency in diagnostic criteria. Consequently, the introduction of continuous glucose monitoring (CGM) as a management tool for prediabetes presents a groundbreaking opportunity to bridge this gap and personalize care, ensuring no individual falls through the preventative net.

CGM's ability to provide continuous, real-time insights into glucose dynamics represents a significant advancement in prediabetes management. By capturing the full extent of glycemic variability, CGM enables healthcare providers to design tailored interventions that address an individual's unique glycemic patterns, thereby optimizing disease prevention efforts and promoting long-term health outcomes. The urgency of prediabetes management is paramount, and the integration of CGM into routine care represents a crucial step toward realizing this goal.

The Power of Continuous Glucose Monitoring

Continuous glucose monitoring (CGM) technology has emerged as a groundbreaking advancement in glycemic control, fundamentally altering our approach to understanding and regulating fluctuations in blood glucose levels. By delivering real-time, uninterrupted data streams of glucose concentrations, CGM provides unprecedented insights into an individual's specific glycemic patterns, surpassing the constraints of conventional intermittent monitoring methods.[10] This technological leap facilitates a more refined and tailored approach to diabetes care, aligning therapeutic interventions with the unique needs of each patient. CGM systems are broadly classified into two categories: retrospectively analyzed and real-time CGM, each designed to address distinct clinical requirements and patient preferences.[11]

Intermittently Scanned CGM (isCGM)

Intermittently scanned CGM systems capture extensive glucose data spanning multiple days to weeks, offering a comprehensive view of glycemic trends.[12] This rich dataset, once downloaded and analyzed, uncovers previously undetected glycemic excursions, particularly postprandial hyperglycemia and nocturnal asymptomatic hypoglycemia, which can significantly impact glycemic control yet are often missed by routine intermittent testing.[13] By revealing these hidden glycemic patterns, isCGM enables a more thorough assessment of glycemic status and informs the development of targeted therapeutic strategies. While lacking the automated alerting capabilities of real-time systems, isCGM offers a flexible and cost-effective option for patients who prefer a more self-directed approach to their glycemic monitoring. This system is particularly suited for individuals with prediabetes who demonstrate confidence in their self-management abilities and desire a proactive role in their glycemic oversight.

Real-Time CGM (rtCGM)

In contrast, real-time CGM technology provides patients instant access to their glucose levels, accompanied by high and low glucose alerts. This feature equips patients to proactively adjust their behaviors in response to real-time glucose readings, effectively mitigating acute glycemic excursions and facilitating precise daily glycemic management.[13] Recent reviews[14,15] have underscored rtCGM's potential in improving glycemic outcomes and preventing diabetes complications. Additionally, rtCGM has demonstrated sensitivity in detecting early glycemic abnormalities, including previously

undiagnosed cases of prediabetes and diabetes.[16] As an educational tool for lifestyle management, rtCGM has proven beneficial in early type 2 diabetes (T2D) or prediabetes, fostering patient empowerment and engagement.

In essence, rtCGM represents the forefront of diabetes management innovation, automatically transmitting continuous glucose data streams to users. This revolutionary capability not only enables patients to stay abreast of their glycemic fluctuations but also triggers timely alerts when blood glucose levels deviate from safe ranges, safeguarding against severe complications.[17,18] Furthermore, rtCGM seamlessly synchronizes detailed glucose data, including trend graphs and numerical values, to various smart devices such as receivers, smartwatches, or smartphones, facilitating remote monitoring and personalized adjustment of dietary, exercise, and medication regimens.[19]

In summary, rtCGM excels with its immediate glucose readings and automated alerts, enabling prompt behavioral adjustments and precise glycemic management, thus reducing the risk of complications. However, it may come with higher costs and a reliance on technology. IsCGM, on the other hand, offers a comprehensive view of glycemic trends over time, is more cost-effective, and suits patients who prefer a self-directed approach, but lacks the real-time feedback and alerts of rtCGM. The choice between the two depends on individual patient needs for real-time intervention versus cost-effectiveness and self-management flexibility. Both isCGM and rtCGM offer valuable tools for glycemic management, each with its unique strengths. While rtCGM excels in providing real-time insights and automated alerts, isCGM remains a viable option for self-directed patients seeking flexibility and affordability. Ultimately, the choice between these systems should be guided by individual patient needs preferences, and clinical goals, ensuring a tailored approach to prediabetes care.

Clinical Implications and Benefits

In the prediabetic phase, while pharmacological intervention is typically unnecessary, effective glycemic control can be achieved through strategic modifications to diet and an increase in physical activity. Nonetheless, recognizing the pivotal role of prediabetes as a precursor to type 2 diabetes (T2D), early detection and proactive management strategies are imperative.

One of CGM's salient advantages lies in its capacity to detect early indicators that may herald the onset of T2D. These include postprandial hyperglycemia, manifested as elevated glucose levels following meals, and the dawn phenomenon, characterized by an overnight rise in blood glucose.[20,21] Both phenomena are common in prediabetes and are associated with an elevated risk of progression to T2D. By identifying these early markers, CGM enables timely intervention, potentially mitigating the risk of disease progression.

Moreover, CGM data provide invaluable insights into an individual's unique glycemic patterns, informing the development of personalized intervention strategies. For example, patients experiencing pronounced postprandial hyperglycemia may benefit from tailored dietary adjustments or targeted exercise programs designed to minimize meal-related glucose excursions. Similarly, those with the dawn phenomenon may require specific guidance on managing overnight glucose levels, potentially through medication adjustments or alternative therapeutic approaches.

Another distinctive strength of CGM is its precision in monitoring glucose variability (GV), a potent independent risk factor for diabetes complications that may even surpass the detrimental effects of sustained hyperglycemia.[22] In prediabetes, GV acts as a crucial biomarker, signifying the transition from normal glucose regulation to impaired glucose tolerance.[23] By incorporating CGM metrics into routine monitoring protocols for prediabetic individuals, we can anticipate the emergence of more effective prevention and management strategies that specifically target GV, thereby slowing or even reversing the progression of diabetes.

Beyond its diagnostic and therapeutic value, CGM fosters a heightened sense of patient engagement and empowerment.[24–26] By affording patients real-time insights into their glycemic status, CGM encourages proactive self-management and deepens their understanding of the intricate relationship between lifestyle choices and glycemic control.[27] This enhanced awareness promotes adherence to therapeutic recommendations and ultimately leads to improved diabetes outcomes.

The Psychological and Behavioral Impact

Beyond its technical advantages, CGM profoundly influences patients' psychological well-being and behavioral patterns. By providing real-time visual feedback on the impact of lifestyle choices on glucose levels, CGM fosters a heightened sense of personal responsibility and awareness.[28] This direct connection between actions and consequences fosters stronger internal motivation to adhere to recommended lifestyle modifications, including dietary adjustments and increased physical activity.[29]

A study in type 1 diabetes (T1D) patients has shown that CGM use significantly enhances quality of life, boosting confidence in blood sugar management and alleviating diabetes-related distress.[29] Similar benefits are anticipated in prediabetes management, where increased self-awareness and behavioral changes driven by CGM data may prove pivotal in reversing prediabetic conditions and reducing diabetes risk.

Challenges and Future Directions

Despite the undeniable potential of CGM in enhancing prediabetes management, several formidable challenges persist that necessitate innovative strategies and ongoing research. Chief among these is the cost barrier, which poses a significant obstacle, particularly in resource-constrained settings.[30,31] To address this, research must delve into cost-effective implementation models that ensure widespread accessibility without compromising patient outcomes. Moreover, ensuring effective CGM utilization necessitates robust training and education programs tailored for both patients and healthcare providers. These programs should emphasize the importance of data interpretation, lifestyle modifications, and the timely adoption of therapeutic interventions based on individual glycemic variability (GV) patterns.

Recent studies[32,33] have found that blood glucose data calibrated by continuous blood glucose monitoring can predict diabetic complications. It is crucial to recognize that prediabetes does not equate to an absence of complications; indeed, research has indicated that prediabetes may be associated with certain complications, like vascular complications.[34–36] Future research endeavors should concentrate on refining CGM algorithms to improve diabetes risk prediction accuracy. This will facilitate earlier identification of those at highest risk and enable more targeted, preventive interventions. Additionally, exploring personalized intervention strategies grounded in individual GV profiles represents a promising avenue for halting or reversing prediabetes progression.

A paradigm shift is underway with the integration of CGM data into broader health monitoring ecosystems, encompassing wearable devices and smartphone apps.[37] Structured biosensor, as a minimally invasive alternative, offer painless transdermal access, fostering the development of more user-friendly wearable CGM devices.[38] This fusion has the potential to revolutionize remote patient management, enabling real-time, data-driven interventions that optimize glycemic control and patient well-being. In the realm of sensor technology, future advancements will focus on improving the accuracy, reliability, and user-friendliness of CGM devices.[39] This will involve the development of more advanced sensors with enhanced biocompatibility, longer lifespans, and improved resistance to environmental interferences. Additionally, efforts will be directed towards minimizing the invasiveness of CGM systems, potentially leading to the development of fully implantable or non-invasive monitoring technologies. A proof-of-concept study[40] demonstrates the feasibility of using non-invasive wearables for glycemic monitoring and highlights the relationship between these wearables and glycemic metrics. The findings revealed that out of the 27 models developed for glucose variability metrics using non-invasive wearables, 11 achieved high accuracy with a mean average percent error (MAPE) of less than 10%. The HbA1c estimation model using non-invasive wearable data achieved a MAPE of 5.1% on the external validation cohort. The methods and findings of this study provide a valuable foundation for future research in this field. Recent research[41] has highlighted the potential of population-specific glucose prediction in diabetes care using transformer-based deep learning approaches implemented on edge devices. This aligns with the emerging trend in CGM, where the integration of AI is becoming a pivotal feature. In line with this progression, Roche has recently released its first predictive AI-enabled CGM device, the Accu-Chek SmartGuide[42], marking a significant advancement in diabetes management.[43] The integration of AI-enabled predictive algorithms allows the system to indicate hypoglycemia risk in the next half hour, forecast glucose level trends over the coming hours, and estimate the risk of nocturnal hypoglycemia.

The introduction of the Accu-Chek SmartGuide, along with continual advancements in glucose prediction models, highlights the future direction of CGM. The fusion of AI and edge computing stands ready to transform diabetes care, facilitating more tailored, proactive, and efficient management approaches.

Within the field of endocrine diabetes, future research will aim to elucidate the complex pathophysiological mechanisms underlying glycemic variability and its association with diabetic complications.[44] This deep dive will pave the way for the discovery of novel therapeutic targets and the crafting of more efficacious treatment strategies. Additionally, by amalgamating CGM data with other biomarkers,[45,46] such as insulin sensitivity and beta-cell function, we will gain a more holistic understanding of diabetes progression, thereby enabling more tailored management approaches.

Furthermore, the advent of artificial intelligence (AI) algorithms tailored to analyze CGM data presents an unprecedented opportunity.[47] These algorithms can decipher complex glycemic patterns, predict future glycemic excursions, and offer personalized recommendations that dynamically adjust to patients' evolving needs.[48]

Conclusion

Given the substantial decline in β-cell function frequently observed at the time of diagnosis in many individuals with prediabetes, their inevitable progression to T2D underscores the critical importance of early identification and detection of high-risk populations.[49] Prediabetes represents a critical juncture in the progression to overt diabetes, necessitating urgent and targeted intervention strategies. CGM, with its ability to provide real-time, continuous glucose monitoring, offers a powerful tool for understanding individual glycemic patterns and guiding tailored therapeutic interventions. Beyond its technical merits, CGM fosters heightened self-awareness and behavioral changes that are integral to reversing prediabetic conditions and reducing diabetes risk.[50] As we navigate the challenges of implementing CGM in prediabetes management, ongoing research and innovation will be essential to unlock its full potential and transform the landscape of diabetes prevention and care. Fundamentally, more concerted efforts are warranted to leverage CGM and other advanced technologies to slow the progression of prediabetes as it is currently defined, which may ultimately decrease the reliance on pharmacologic interventions and mitigate the substantial socio-economic burden associated with this condition.

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