

Diabetologists' and Patients' Views on Continuous Glucose Monitoring: Do They Talk about the Same Story?

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Abstract

As clinicians, we believe that patients with diabetes have the same views on continuous glucose monitoring that we have. For them, however, the focus is not optimization of metabolic control, but living a life that is as normal as possible. This difference can become an issue in clinical trials of systems for continuous glucose monitoring. If such systems demonstrate no benefit to metabolic control over standard spot capillary glucose monitoring, does this really reflect an insufficient efficacy of the continuous glucose monitoring system tested or is this the result of a "conflict of interest?" This commentary contemplates the mismatch in aims that might lead to such study results. From my point of view, it is critical to find a solution to this issue, as otherwise the benefits of continuous glucose monitoring (which I believe in quite strongly) cannot be shown in a manner that convinces health care payers to reimburse these new technologies on a broader scale.

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Continuous Glucose Monitoring (CGM): Still in Its Infancy or Something for Daily Care?

With a view on the great enthusiasm regarding CGM at the recent American Diabetes Association (ADA) in Chicago, I'm wondering about the current status of this novel diagnostic tool for diabetes therapy. Is it a full-blown technology that can be used for daily care of each and every patient with diabetes (as some people/companies would like to make us believe) or is it a highly unreliable "toy" that until now has not shown

in convincing randomized controlled trials (RCTs) to have a real benefit for the patients? Concerning the high cost of this technology, this is an important and very relevant question. However, in order to provide a clear answer on the question raised (and to convince the health insurance companies to reimburse the use of CGM), appropriately designed and performed RCTs are necessary.

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Abbreviations: (ADA) American Diabetes Association, (AUC) area under the curve, (CGM) continuous glucose monitoring, (HbA1c) hemoglobin A1c, (MBG) mean blood glucose, (RCTs) randomized controlled trials

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Randomized Controlled Trials and CGM

Therefore, companies such as Medtronic have initiated RCTs like the series of three STAR studies. At the ADA the results of the STAR 1 study were presented very eloquently by its principal investigator, Dr. Irl Hirsch. However, the “negative” outcome of this study was not the one I had anticipated (and hoped for): The quality of metabolic control was not different between the group of patients using the Guardian® RT for CGM and the other group of patients using self-monitoring of blood glucose. There was a benefit with respect to hypoglycemic events while wearing the CGM system; however, no significant differences in the primary variable mean no significant differences! My question to Irl, directly after his presentation, was about his best explanation for the study outcome and his simple answer was: The patients do not use the device as often as they should! To sharpen this critical aspect even more, we have to take into account that patients willing to participate in a clinical trial represent a highly select group of motivated patients and the same holds true for diabetologists working as investigators in such trials; it is understandable if “standard” patients might be even more reluctant to use CGM systems in daily life!

“Better” RCTs in the Future?

Will we ever have RCTs showing convincingly a “positive” outcome when we can't motivate patients to make more use of this new technology in daily life? Health care providers are reluctant to reimburse CGM systems without proof of a sufficient medical benefit/reduction of other costs (e.g., lower costs for treatment of diabetes-related late complications). Without reimbursement, this whole development might not progress (if it does at all) at the speed that all of us (also the patients!) would like to see.

As a result, we have to ask ourselves the following question: are the “medical” benefits that can be achieved by the use of CGM identical for patients and diabetologists? Currently, most RCTs are focusing on more or less the same end points as in studies for the development of new antidiabetic drugs [hemoglobin A1c (HbA1c), frequency of hypoglycemic events, quality of life]. This is probably because regulatory authorities and health care payers ask for these numbers because, like us, they regard them as relevant parameters.

In recent studies for the evaluation of the clinical performance of CGM systems, other parameters were also studied:

- Mean blood glucose (MBG)
- Minimal and maximal blood glucose
- Amplitude/variability
- Measurements of swings
- M value
- Standard deviation of MBG
- Mean amplitude of glycemic excursions
- Mean indices of meal excursions
- Mean of daily differences
- Area under the curve (AUC) under the glucose profile in total
- AUC/time spend in low/high blood glucose range
- Composite parameter describing glucose profiles in a single number, e.g., %PRESS
- Nocturnal glucose control
- Fasting ascending glycemic excursion

Such a long listing (which is not exhaustive!) raises the suspicion that apparently there is no good single parameter (at least not one all of us have agreed upon) that describes the clinical advantages of CGM systems in an optimal manner! It does not appear easy to transform the huge amount of information provided by CGM systems about the daily glucose profiles into a single parameter that describes all aspects of glucose profiles in an easy-to-interpret manner.

At the end the question remains: are patients interested in these parameters? Probably for patients, a trend analysis of the current glucose profile that allows them to counteract a declining blood glucose adequately early enough—before it converts into a hypoglycemic event—is much more relevant. However, is a reliable hypoglycemic warning system something a health care payer is willing to pay for? A given patient is probably not interested in statistical parameters describing the quality of glucose monitoring in a given group of patients in a study (performed somewhere in the world); he is interested in the measurement quality in his individual case on a given day in his daily life. Such a patient will be frustrated by too many false positive alarms during the night that have woken him up over and over again without a confirmatory low capillary blood glucose level if the hypoglycemic warning system is not reliable enough. If this is the case, he will simply switch off the alarm or not use the CGM system during the night.

Please keep in mind that it might not be only the patient that was waking up in the middle of the night by the alarm of the CGM system but also another person in the same bed. Would your wife/husband tolerate this if no good reason exists?

Patients Demand for CGM

In view of the fact that patients (and the lay groups) have aggressively asked for the development of CGM by scientists and companies for many years (decades?), one wonders why the patients do not use such systems very enthusiastically once they become available. One simple reason for the reluctance to use new CGM systems may be that patients are not willing/able to pay the relatively high prices for these novel systems! Patients have learned to treat their diabetes more or less well by measuring capillary blood glucose levels several times per day, which is combined with costs in the range of some dollars per day. To increase this financial burden might be a hurdle, even if the promises of CGM are high: a full overview of the daily blood glucose profile, no acute metabolic deteriorations, easier optimization of metabolic control, and so on. However, with a view on the results of the STAR 1 study, the costs of CGM usage are not an argument in the framework of a clinical trial in which the sponsor of such a study usually covers all costs.

Another good reason for patients not to use the recent CGM systems that fanatically is that these systems are too cumbersome to use, not reliable enough, and not easy to wear. In other words, the current CGM systems are probably not the ones the patients would like to have!

I would like to point out one aspect that might be troublesome for patients: Imagine that you are a pump user—you have to wear the insulin pump, the CGM system, and a blood glucose meter with test strips to carry around. Most probably you will have in addition a mobile phone and a MP3 player. Can you imagine all the connection lines, batteries, and so on that you will have to take care of? Not only do you have to carry a lot of equipment, all these systems are supposed to work properly all the time under all conditions that daily life offers. Is this something a scientist/engineer has in mind when he develops a new CGM system?

Communication between Patients and Diabetologists/Companies

If patients do not use a technology that diabetologists believe will help them greatly, the question is, is there

a fundamental “misunderstanding” between both groups? Do we have a clear understanding of patients' expectations toward CGM systems? I can see all my colleagues nodding their head and saying clearly I know what my patients want. Please be careful and not be too self-confident, as the experience of the STAR 1 study (and probably that of others as well) tells another story!

Let me mention one aspect that highlights the different view of diabetologists and patients: Patients have an extremely high desire for discretion; they do not want it to be obvious that they are different/ill. Therefore, for patients, the size/shape of a CGM system is highly relevant. In contrast, diabetologists may regard size as not of paramount importance but regard a high measurement quality system as much more important. Clearly, the ideal CGM system would combine the wishes of both groups at the same time. If this, however, is not possible, on which side should we put our focus?

Summary

From my point of view, CGM is an important step forward not only per se but for the progress of diabetes technology as its own area of research in general. I'm sure that we will see diabetes technology as becoming a fully accepted and integrated part of diabetes therapy in the near future. However, it will be a critical aspect to integrate the view of patients with diabetes fully into this development. Otherwise we might end up in a dilemma: patients will use CGM systems in a manner that helps them ease their daily struggle with diabetes therapy, but does not really aim for an optimization of metabolic control (=reduction of HbA1c). Subsequently, the health care payers will say that a CGM system is an expensive toy that does not induce a clinically relevant benefit (=no reimbursement). We should try to establish a platform that allows patients to bring their practical aspects and demands to the table at an early stage. If we are able to integrate all the different aims/views into one in order to talk about the same story, not only will this promote the development of CGM systems, but also this area of research in general.

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This commentary is a summary of thoughts and aspects that I have discussed with many colleagues in the past years. Many of them were also discussed during scientific advisory board meetings with different companies that I have had the chance to attend. For such meetings and oral presentations I have received honoraria. Profil Institute for Metabolic Research has performed a number of clinical trials in this area of research with numerous companies over the last 9 years. I am one of the two CEOs of this company and a shareholder.