

Risk Probability of Having Cardiovascular Disease Resulted from the Combination of Metabolism Index and Glucose Fluctuation using a Continuous Glucose Monitoring Sensor Collected Daily Glucose Data over 1,170 Days Based on GH-Method: Math-Physical Medicine (No. 483)

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Abstract

Recently, the author read an article published in the medical journal of *Cardiovascular Diabetologist* on July 4, 2020, and selected the following excerpt:

“Although Glycemic variability (GV) remains yet no consensus, accumulating evidence has suggested that GV, representing either short-term (with-day and between-day variability) or long-term GV, was associated with an increased risk of diabetic macro-vascular and microvascular complications, hypoglycemia, mortality rates and other adverse clinical outcomes.”

The author has selected a few excerpts from other research papers regarding the subject of glycemic variability (GV). Of course, the advantages of using glucose fluctuations (GF) has become easier due to the wide acceptance of the continuous glucose monitor (CGM) sensor device for diabetes patients in recent years.

Due to his personal preference, he uses the term of “GF” instead of “GV” in his medical research work due to GF’s non-ambiguity of definition and ease-of-calculation from glucose data directly. In addition, both of the short-time frame of within-day GF, between-day GF, and long-time frame of GF are considered and incorporated in his combined GF model.

In this article, he attempts to define a combined arithmetic formula for GF which includes the following five glucose components: sensor daily glucose (eAG), daily GF over 24 hours (daily GF), postprandial plasma glucose GF over 3 hours (PPG-3 GF), PPG GF over 2 hours (PPG-2 GF), and fasting plasma glucose GF over 7 hours (FPG GF).

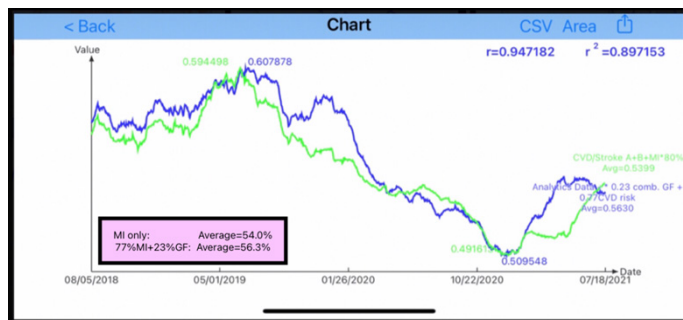
In previous research work, his calculated risk probabilities of having different types of diabetic complications, including cardiovascular disease (CVD), over a long period of time have been fundamentally based on a model of using the overall metabolism index (MI). This “MI-only” model consists of 10 general categories with 500 detailed elements. However, it did not take any consideration of GF, either slower-term GF within-day, within-meal, between-day, or long-term GF.

Recently in 2021, he starts introducing the GF factor into his research work, instead of using the average glucose values only, such as HbA1C, into his risk assessments of diabetic complications. In other words, by including this additional influential factor of a combined GF score into his existing MI-based risk assessment models, he expects to see more insight from this diabetes influence factor of GF on risks probability of having CVD.

In summary, the results from the comparison study between MI-only model (average risk level at 54%) and MI plus GF model (average risk level at 56.3%) is a small CVD risk difference of 2% over this period of 1,170 days. However, by further examining the daily diagram closely, some of the “local Risk deviations” are greater when the patient has more significant and larger amount of GF. This makes perfect biomedical and biophysical sense that a higher GF is indeed associated with a higher amount of energy, where higher-energy can impact and damage internal vital organs such as the heart or brain.

Based on the interesting findings from his research work regarding the file of GF and its impact, the author began focusing not only on his daily estimated HbA1C levels but also on the cal-

culated GF magnitudes via CGM Glucose readings. Under the newly introduced element of GF into his iPhone APP, he has reached another level of his daily glyceemic control for his type 2 diabetes.



Introduction

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assessment models, he expects to see more insight from this diabetes influence factor of GF on risks probability of having CVD.

Methods

MPM Background

To learn more about his developed GH-Method: math-physical medicine (MPM) methodology, readers can read the following three papers selected from the published 400+ medical papers.

The first paper, No. 386 describes his MPM methodology in a general conceptual format. The second paper, No. 387 outlines the history of his personalized diabetes research, various application tools, and the differences between biochemical medicine (BCM) approach versus the MPM approach. The third paper, No. 397 depicts a general flow diagram containing ~10 key MPM research methods and different tools.

In short, the author studies and analyzes various digital footprints of human disease’s biophysical phenomena using academic tools he has learned about mathematics, physics, engineering, and computer science.

The Author’S Diabetes History

The author was a severe type 2 diabetes patient since 1996. He weighed 220 lb. (100 kg) at that time. By 2010, he still weighed 198 lb. with an average daily glucose of 250 mg/dL (HbA1C at 10%). During that year, his triglycerides reached to 1161 (high risk for CVD and stroke) and albumin-creatinine ratio (ACR) at 116 (high risk for chronic kidney disease). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding the needs of kidney dialysis treatment and future high risk of dying from his severe diabetic complications.

In 2010, he decided to self-study endocrinology with emphasis on diabetes and food nutrition. During 2015 and 2016, he developed four mathematical prediction models related to diabetes conditions: weight, postprandial plasma glucose (PPG), fasting plasma glucose (FPG), and HbA1C (A1C). Through using his developed mathematical MI model and the other four glucose prediction tools, by the end of 2016, his weight was reduced from 220 lbs. (100 kg) to 176 lbs. (89 kg), waistline from 44 inches (112 cm) to 33 inches (84 cm), average finger-piercing glucose from 250 mg/dL to 120 mg/dL, and A1C from 10% to ~6.5%. One of his major accomplishments is that he no longer takes any diabetes related medications since 12/8/2015.

In 2017, he had achieved excellent results on all fronts, especially his glucose control. However, during the pre-COVID period, including both 2018 and 2019, he traveled to ~50 international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control caused by stress, dinnning out frequently, post-meal exercise disruption, jet lag, along with the overall negative metabolic impact from the irregular life patterns; therefore, his glucose control was somewhat affected during the two-year traveling period of 2018-2019.

He started his self-quarantined life on 1/19/2020. By now, 7/15/2021, his weight was further reduced to ~165 lbs. (BMI 24.4) and his A1C was at 6.2% without any medications intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written

more than 200 new research articles and published a total of 400 medical papers in various medicine and engineering journals, but he has also achieved his best health conditions for the past 26 years. These achievements are resulted from his non-traveling, low-stress, and regular daily life routines. Of course, his in-depth knowledge on chronic diseases, sufficient practical lifestyle management experiences, and his own developed high-tech tools have also contributed to his excellent health improvements.

On 5/5/2018, he applied a continuous glucose monitoring (CGM) sensor device on his upper arm and checks his glucose measurements every 5 minutes for a total of 288 times each day. He has maintained the same measurement pattern to present day. However, in his research work, he decides to use the 15-minute sensor collected glucoses (96 data per day) due to its high accuracy and lower cost on computations.

During the past 11.5 years, he has continuously investigated, studied, and analyzed his collected more than 2 million data regarding his health status, medical conditions, and lifestyle details. He applies his physics knowledge, engineering models, mathematical tools, and computer programming to conduct his medical research work. His entire medical research work is based on the aims of achieving both “high *precision*” with “*quantitative* proof” in the bio-medical findings, not just through linguistic expressions with qualitative words, vague statements, or complex medical terminologies. His personal goal is to his own life through research, and then helping family members along with other patients through distributing his knowledge learned and experiences gained from his 11.5 years medical research work to combat these chronic diseases and complications at the root-cause level.

It should be noted that the author uses a CGM sensor device which adopts the flash glucose monitoring (FGM) method. The following is an excerpt from diaTribe Learn (diatribe.org):

Flash Glucose Monitoring

What It Does: Flash Glucose Monitoring (FGM) is the newest method of glucose testing that is seen as a hybrid between meters and CGMs. The Abbott FreeStyle Libre is currently the only flash glucose monitoring product available, and it is currently only approved in Europe. In Flash Glucose Monitoring, patients have a sensor inserted on their upper arm and a separate touch-screen reader device. When the reader device is swiped close to the sensor, the sensor transmits both an instantaneous glucose level and eight-hour trend graph to the reader. This allows people to get individual blood sugar readings (like BGM) and trend information (like CGM). However, unlike CGM, FGM does not have hypo- or hyperglycemia alarms and will only provide a trend graph if it has been swiped in the past eight hours.

The FreeStyle Libre system does not require finger-stick calibration, so users can dose insulin based on its readings (except for when hypoglycemic, when glucose levels are rapidly changing, or when symptoms don't match the system's readings).”

Diabetic Complication Risk Model based on Overall Metabolism

In 2014, the author applied topology concept, finite-element engineering technique, and nonlinear algebra operations to develop a complex mathematical model of metabolism. This model

contains 10 categories, including four output categories (weight, glucose, blood pressure, and lipids), and six input categories (food, water intake, exercise, sleep, stress, and routine life patterns). These 10 categories are comprised of approximately 500 detailed elements. He also defined two new parameters: metabolism index or MI, as the combined score of the above 10 metabolism categories and 500 elements along with the general health status unit (GHSU), as the 90-days moving average value of MI. Since 2012, he has collected more than 2 million data of his own biomedical conditions and personal lifestyle details.

Following the mathematical metabolism model, he further developed a series of models regarding diabetic complications which contain some detailed equations to predict his risk probabilities of having a stroke, CVD, chronic kidney diseases (CKD), pancreatic beta-cells self-recovering assessment, and diabetic retinopathy (DR). These risk assessment models include a patient's baseline data including age, race, gender, family genetic history, medical history, and bad habits which contribute approximately 20% to the total risk. Furthermore, it also includes the following two major areas each with a 40% contribution:

- (1) Medical conditions - individual M1 through M4 which include obesity, diabetes, hypertension, hyperlipidemia and others. It should be emphasized here that diabetes (i.e., glucose) alone contributes about 20% of the total risk.
- (2) Lifestyle details - individual M5 through M10 which affect medical conditions.

In addition, he also uses his defined two terms, MI and GHSU, as a combined score of M1 through M10 and 90-days moving average MI, for his calculation. Of course, all of these 10 metabolism factors (m1 through m10) are inter-related. The “break-even line” between healthy state and unhealthy state for both MI and GHSU is 0.735 or 73.5%.

With this mathematical risk assessment model, he can obtain three separate risk probability percentages associated with each of the three calculations mentioned above. As a result, this model would offer a range of the risk probability predictions of having a diabetic complication based on the patient's metabolic disorder conditions, unhealthy lifestyles, and the combined impact on the body.

Other GV Research Work

There are many available articles regarding the subject of glycemic variability (GV), however, the author decides to include the following combined excerpt from two particular published articles (References 4, 5, and 6). These three references have cited a total of 114 published papers. In this way, readers do not have to search for key information from a long list of their cited reference articles. Reference 4 focuses on comparison of many published GV articles. Reference 5 concentrates on algorithm, method and firmware design of a web-based APP software for calculating GV values.

Here is the Combined Excerpt:

“Several pathophysiological mechanisms were reported, unifying the two primary mechanisms: excessive protein glycation end products and activation of oxidative stress, which causes vascular complications. Intermittent high blood glucose exposure, rather than constant exposure to high blood glucose, has

been shown to have deleterious effects in experimental studies. In in-vitro experimental settings and in animal studies, glycemic fluctuations display a more deleterious effect on the parameters of CV risk, such as endothelial dysfunction. There is a significant association between GV and the increased incidence of hypoglycemia. Hypoglycemic events may trigger inflammation by inducing the release of inflammatory cytokines. Hypoglycemia also induces increased platelet and neutrophil activation. The sympathoadrenal response during hypoglycemia increases adrenaline secretion and may induce arrhythmias and increase the cardiac workload. Underlying endothelial dysfunction leading to decreased vasodilation may contribute to CV risk. Published studies have demonstrated that **GV, particularly when associated with severe hypoglycemia, could be harmful not only to people with diabetes but also to non-diabetic patients in critical care settings.** Overall, the pathophysiological evidence appears to be highly suggestive of **GV being an important key determinant of vascular damage.** Growing evidence indicates that significant GV, particularly when accompanied by hypoglycemia, can have a harmful effect not only on the onset and progression of diabetes complications but also in clinical conditions other than diabetes treated in intensive care units (ICUs). **In addition to HbA1c, GV may have a predictive value for the development of T1DM complications. In insulin-treated T2DM, the relevance of GV varies according to the heterogeneity of the disease, the presence of residual insulin secretion and insulin resistance. HbA1c is a poor predictor of hypoglycemic episodes because it only considers 8% of the likelihood of severe hypoglycemia; on the contrary, GV can account for an estimated 40% to 50% of future hypoglycemic episodes. HbA1c is a poor predictor of hypoglycemic risk, whereas GV is a strong predictor of hypoglycemic episodes. GV was an independent predictor of chronic diabetic complications, in addition to HbA1c. We should note that PPG and GV are not identical, even if they are closely related. The attention dedicated to GV is derived from the above evidence concerning its effects on oxidative stress and, from the latter, on chronic diabetes complications. Control of GV has been the focus of a number of interventional studies aimed at reducing this fluctuation. Diet and weight reduction are the first therapeutic instrument that can be used for reducing GV.**

Despite the various formulas offered, simple and standard clinical tools for defining GV have yet to evolve and different indexes of GV should be used, depending on the metabolic profile of the studied population. Moreover, the absence of a uniformly accepted standard of how to estimate postprandial hyperglycemia and GV adds another challenge to this debate.

The majority of these studies have used time-averaged glucose values measured as glycosylated hemoglobin (HbA1c), an indicator of the degree of glycemic control, which is why HbA1c has become the reference parameter for therapies aimed at reducing the risk of complications from diabetes. **Chronic hyperglycemia is almost universally assessed by HbA1c which has been shown to correlate closely with mean glucose levels over time, as determined by continuous glucose monitoring (CGM).** However, the relative contribution of postprandial glycemic excursions and fasting to overall hyperglycemia has been the subject of considerable debate. Monnier et al. suggested that the relative contributions of fasting and postprandial glucose differ according to the level of overall glycemic control. **Fasting glucose concentrations present the most important contribution to hemoglobin glycosylation, whereas at lower levels of**

HbA1c, the relative contribution of postprandial hyperglycemia becomes predominant. Collectively, GV is likely to be incompletely expressed by HbA1c, particularly in patients with good metabolic control.

GV is a physiological phenomenon that assumes an even more important dimension in the presence of diabetes because it not only contributes to increasing the mean blood glucose values but it also favors the development of chronic diabetes complications. **It appears that GV is poised to become a future target parameter for optimum glycemic control over and above standard glycemic parameters, such as blood glucose and HbA1c. Avoiding both hyperglycemia and hypoglycemia by careful use of SMBG and the availability of new agents to correct hyperglycemia without inducing hypoglycemia is expected to reduce the burden of premature mortality and disabling CV events associated with diabetes mellitus. However, defining GV remains a challenge primarily due to the difficulty of measuring it and the lack of consensus regarding the most optimal approach for patient management.**

The risk of developing diabetes-related complications is related not only to long-term glycemic variability, but may also be related to short-term glucose variability from peaks to nadirs. Oscillating glucose concentration may exert more deleterious effects than sustained chronic hyperglycemia on endothelial function and oxidative stress, two key players in the development and progression of cardiovascular diseases in diabetes. Percentages of hyperglycemia (levels between 126 and 180 mg/dl) and hypoglycemia (levels below 70.2 mg/dl) episodes should be used in the GV related research. **Mean amplitude of glycemic excursions (MAGE), together with mean and SD, is the most popular parameter for assessing glycemic variability and is calculated based on the arithmetic mean of differences between consecutive peaks and nadirs of differences greater than one SD of mean glycemia. It is designed to assess major glucose swings and exclude minor ones.**

The features discouraging use of glycemic variability as a parameter in clinical practice and trials are the difficulty of interpreting numerous parameters describing this phenomenon and a limited number of computational opportunities allowing rapid calculation of glycemic variability parameters in CGM data.

The UK Prospective Diabetes Study (UKPDS) showed that after an initial improvement, glycemic control continues to deteriorate despite the use of oral agents to enhance insulin secretion and to reduce insulin resistance. This deterioration can be attributed to the progressive decline of β -cell function. Even in subjects with well-controlled type 2 diabetes, 70% of the variability of A1C can be explained by abnormalities in postprandial glucose. Chronic sustained hyperglycemia has been shown to exert deleterious effects on the β -cells and the vascular endothelium. Monnier et al. and Brownlee and Hirsch have recently emphasized that **another component of dysglycemia, i.e., glycemic variability, is even more important than chronic sustained hyperglycemia in generating oxidative stress and contributing to the development of secondary diabetes complications.** In vivo studies have convincingly demonstrated that hyperglycemic spikes induce increased production of free radicals and various mediators of inflammation, leading to dysfunction of both the vascular endothelium (3) and the pancreatic β -cell.”

The author read an interesting article published in the Cardiovascular Diabetologist on July 4, 2020: "Glycemic variability: adverse clinical outcomes and how to improve it?" and selected the following excerpt:

"Glycemic variability (GV), defined as an integral component of glucose homeostasis, is emerging as an important metric to consider when assessing glycemic control in clinical practice. **Although it remains yet no consensus, accumulating evidence has suggested that GV, representing either short-term (with-day and between-day variability) or long-term GV, was associated with an increased risk of diabetic macro-vascular and micro-vascular complications, hypoglycemia, mortality rates and other adverse clinical outcomes.**

Glycemic variability (GV), referring to oscillations in blood glucose levels, is usually defined by the measurement of fluctuations of glucose or other related parameters of glucose homeostasis over a given interval of time (i.e., within a day, between days or longer term). Although HbA1c was traditionally considered as the gold standard for assessing glycemic control, GV is a more meaningful measure of glycemic control than HbA1c in clinical practice, and is without doubt now being recognized. Despite its clinical significance, there is no consensus on the optimum method for characterizing GV.

GV and Diabetic Macrovascular and Microvascular Complications

Given that the limitations of HbA1c measurements, growing evidence demonstrated that GV was a significant and clinically meaningful glycemic metric and had drawn attention for its effects on adverse clinical outcomes, including diabetic macro-vascular and microvascular complications, hypoglycemia and mortality (Table 2). There is considerable evidence to support the negative role of GV in the development of diabetic macro-vascular and microvascular complications.

GV and Hypoglycemia

Hypoglycemia is the major impediment to therapy in diabetes. While HbA1c remains widely used as a measure of mean glycemia, it may not be the best marker for predicting hypoglycemia. The consolidated evidence to date supported the importance of GV with respect to predicted risk of hypoglycemia. Zinman et al. concluded that **higher day-to-day FPG variability was associated with increased risks of severe hypoglycemia and all-cause mortality.**

GV and Mortality

A number of studies verified that GV was not only associated with the risk of diabetes-related complications and hypoglycemia, but also simultaneously related to the high incidence of mortality. Interestingly, several studies proposed an independent association of GV with mortality. **Clinical data indicated that FPG variability might be an important predictor of mortality, particularly for those with their glycemic status uncontrolled. Besides, in hospitalized patients, increased GV was associated with a higher rate of mortality.** Recently, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, researchers found that HbA1c variability was a strong predictor of all-cause mortality, and this observation was more remarkable in older people with diabetes.

In addition to the above adverse clinical outcomes, GV was also

reported to be associated with depressive symptoms, cognitive disorder and even cancer. In the Israel Diabetes and Cognitive Decline (IDCD) study, GV measured as the SD of HbA1c increased the risk of depressive symptoms. A Taiwan diabetes study explored the relationship between GV and the incidence of Alzheimer disease (AD) in patients with type 2 diabetes mellitus, finding that **GV had a worse impact on AD and might be significant predictors for AD.** More importantly, recent study demonstrated that HbA1c variability was a potential risk factor for later tumorigenesis in patients with diabetes, which might be mediated by oxidative stress or hormone variability.

Conclusion and Future Perspective

We have attempted to summarize the relationships between two categories of GV and the risk for diabetic macrovascular and microvascular complications, hypoglycemia, mortality and other adverse clinical outcomes (Fig. 2). We also generalized the potential beneficial measures including drugs combined with CGM, dietary interventions and exercise training, to improve GV. These findings highlight the important role of GV in the patients with diabetes and provide the essential help for clinicians to manage the blood glucose.

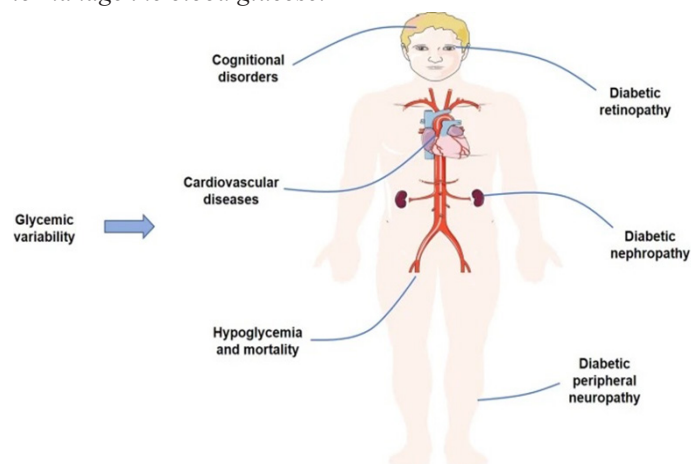


Figure: The effects of glycemic variability on the adverse clinical outcomes.

GV has been identified to be closely associated with the risk of adverse clinical outcomes and provides a better predictor of such complications. However, it still lacking a clear universal definition and different indices have been proposed to evaluate it. With the availability of CGM in clinical practice, the assessment of GV became not only possible but also required. Also, CGM was frequently superior to continuous subcutaneous insulin infusion and could guide individuals' therapeutic changes to reduce GV, hypoglycemia and CVD. **A recent study reported that "flash glucose monitoring", a new approach to glucose monitoring, has a long sensor lifetime of 14 days and emerged as a practical solution to the glucose monitoring.** Meanwhile, a real-world data from Spain indicated that flash glucose monitoring allowed frequent glucose checks and reduced GV, as well as hypoglycemia. Consequently, in order to provide a more comprehensive assessment of GV, the new approach of glucose monitoring is advocated to adopt in clinical practice. **Future developments in new technologies, such as CGM systems and flash glucose monitoring, and indices for better deciphering and defining GV should contribute to improve understanding of the clinical relevance of GV in the management of diabetes.**

Although GV had drawn attention for its effects on diabetic macrovascular and microvascular complications, hypoglycemia and mortality, several studies have shown conflicting results. Caprnda et al. failed to show the association between diabetic complication and GV in patients with type 2 diabetes. Furthermore, in the Diabetes Control and Complications Trial, within-day GV, as determined from quarterly glucose profiles, did not play an explicit role in the development of microvascular complications. However, we found that these results employed the 7-point glucose profiles, which might be insufficient to characterize GV correctly when compared with CGM. Thus, these negative results may not necessarily disprove the importance of GV in the development of diabetic complications. Additionally, the mechanisms linking GV and related complications risk remained unclear. Recent studies corroborated that GV was correlated with oxidative stress or erythrocyte membrane stability, emphasizing its participation in the pathogenesis of related complications. Further prospective research to explore the explicit mechanisms linking GV and related complications is warranted.

Finally, setting clear definitions and taking potential beneficial measures for addressing GV is essential. Further research in these domains will contribute to blood glucose control and management.”

Glucose Fluctuations (GF) or Glycemic Variability (GV)

The concept and practice of GV have existed since the clinical usage of CGM devices to monitor severe diabetes patients and insulin treatments in hospitals. Many medical papers have been published on GV; however, there is no universally accepted formula or equation for generally accepted applications.

Defining GV remains a challenge primarily due to the difficulty of data collection with its associated data cleaning, processing, comprehension and interpretation of the results by physicians and patients along with no consensus regarding the optimal approach for its clinical management. For example, the GV derivation involves the usage of standard deviation (SD) from statistics. Although SD is widely used, it has limitations because the assumption of measured glucose data are normally distributed (similar to a Gaussian distribution), which is typically not the case for bio-waves and medical data. Besides, many research articles use glucose data collected within a few days from hospitalized patients rather than use glucose data collected over a long period, such as years. The reason is that until recently, after 2016-2017, the CGM sensor devices became available to out-patients to collect their own glucose data at home, instead of in the hospitals or clinics. However, the tasks of glucose data transfer from CGM device to a computer and then the necessary follow-on tasks of data processing, data management, and data analysis still remain a challenge, particularly for out-patients. Due to the lack of professional training and academic knowledge in this domain, most patients and clinical physicians have encountered difficulties with these tasks. Data without careful cleaning and proper preparation would create a situation of “garbage inputs” result into “garbage outputs” which fits the common expression in computer science industry of “garbage in and garbage out”.

Based on the above-mentioned theoretical and technical viewpoints, the author decided to conduct his study on “just” applying the basic concept of glycemic variability (i.e., glucose fluctuation between peak and nadir), and without touching certain

created terms or derived formulas by some research doctors described in some of their publications. However, the author further combined the primary characteristics of wave theory, e.g. frequency, amplitude, and wavelength along with the concept of energy theory to include the estimated energy associated with the glucose fluctuations.

He decided to abandon the usage of this term of “glycemic variability or GV” and directly utilize the term of “glucose fluctuations (GF)” in his research work where GF equals to the value of maximum glucose minus minimum glucose. Not only does the simpler definition and form of GF provide a straightforward interpretation and easier comprehension to be applied by both physicians and patients, but it also fully represents the meaning of glycemic variability. The word “variability” can involve and signify many various things to different people.

GV or GF can be applied to many clinical cases with greater mortality for those in intensive care unit or at-home showing increased rate and risk of diabetes complications, and postprandial beta-cell dysfunction (insulin health).

Input Data and Formula of GF

The author has collected 288 glucose data per day (every 5 minutes) and extracted 96 Glucose data per day (every 15 minutes) from the CGM sensor device and then entered them into his computer software since 5/5/2018. He has chosen 1,170 days from a long period of 3+ years (5/5/2018-7/18/2021) for this specific analysis project.

In addition to his daily sensor glucose, eAG, he calculates 4 additional sets of his GF values (maximum glucose minus minimum glucose): daily GF, PPG GF within 3-hour duration, PPG GF within 2-hour duration, and FPG GF within 7-hour duration (from midnight to 7am). This effort results into a total of 4,668 GF data each day. The reason he selects these two sets for PPG GF is that their waveforms are different. The impacts from both food and exercise on glucose would last longer in the blood system than the conventional thinking of two hours. In general, the two-hour waveform is similar to a mountain shape with its peak around 60-minutes and trough at either 0-minute or 120-minutes. However, the three-hour waveform will either have a continuously drop-downward shape from the second hour into the third hour or behaving with a slightly tilt-upward shape at times. Therefore, their GF values are different and the PPG 3-hour GF is usually bigger than the PPG 2-hour GF.

The simple and straightforward arithmetic formula of his “Combined GF” is:

$$\text{Combined GF} = ((eAG/120) + (\text{daily GF}/85) + (\text{PPG 3-hours GF}/70) * (9/24) + (\text{PPG 2-hours GF}/30) * (6/24) + (\text{FPG GF}/35) * (7/24)) / 5$$

In this daily risk assessment study, he further defines his risk probability of having a CVD or Stroke as follows:

Risk Probability

$$= 77\% * \text{daily MI} + 23\% * \text{daily combined GF}$$

Results

The top diagram in Figure 1 shows the daily CVD risk curve using MI+GF model. The middle diagram in Figure 1 depicts the

90-days moving average CVD risk curve using MI+GF model. The bottom diagram in Figure 1 reflects two 90-days moving average curves of MI curve and CVD risk curve which has an extremely high correlation of 99.9%. This is not a surprising finding since the CVD risk contains 77% of MI input.

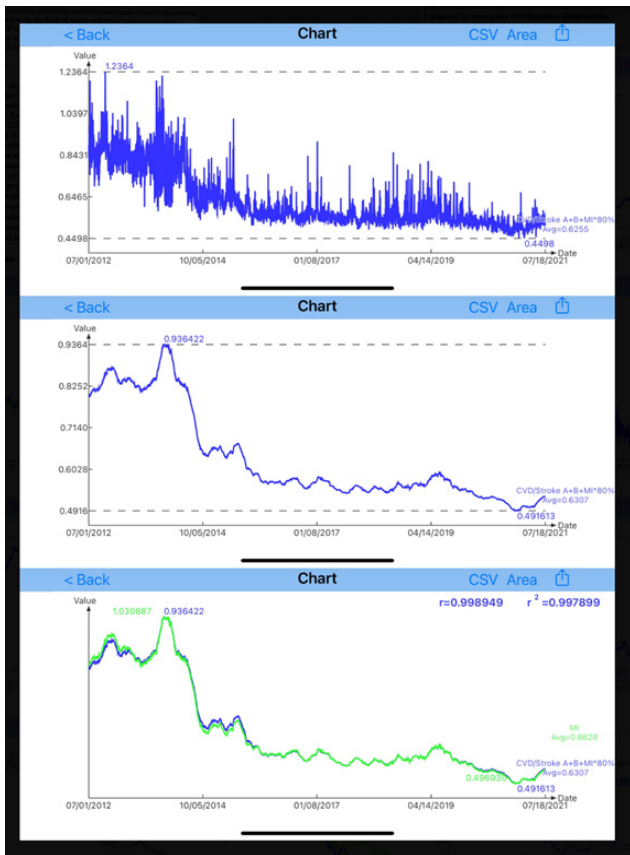


Figure 1: CVD risk curve using MI-only and the MI curve

The top diagram in Figure 2 reveals the 90-days moving average CVD risk using MI+GF model. The middle diagram in Figure 2 shows the 90-days moving average combined GF model. The bottom diagram in Figure 2 signifies the comparison between 90-days moving average CVD risk using MI+GF model versus the 90-days moving average combined GF with a moderate correlation of 55%. This is also not a surprising finding due to the

two waveforms as being quite different in both nature and appearance. The finding further demonstrates the GF factor as a different beast with its own behavior pattern. When T2D patients are able to control their average glucose, such as HbA1C, this does not indicate that their GF is automatically under control; even though, these two parameters do have some correlation in between.

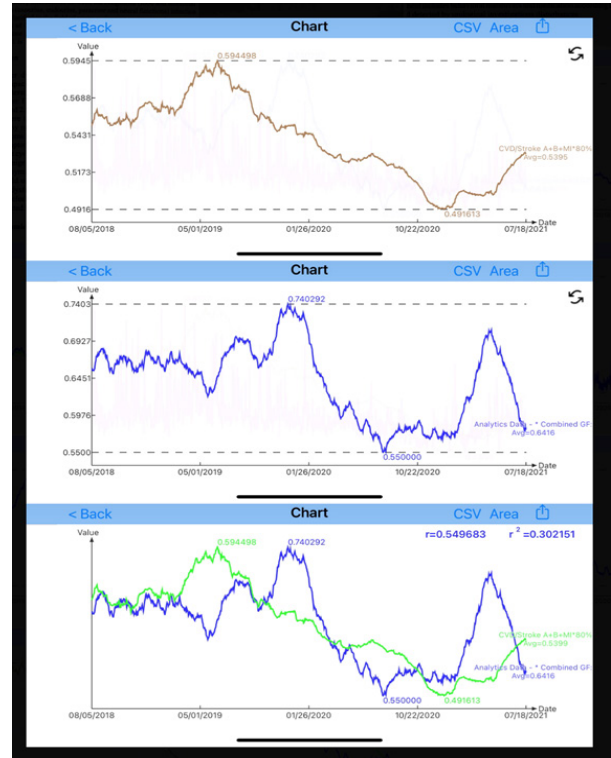


Figure 2: CVD risk curve using MI-only and the Combined GF curve

The top diagram in Figure 3 demonstrates the CVD risk using MI-only model, whereas the middle diagram confirms the CVD risk using the model of 77% MI plus 23% GF. As for the bottom diagram, it uncovers the comparison between the CVD risk using MI-only versus using 77% MI plus 23% GF model with a very high correlation of 95%.

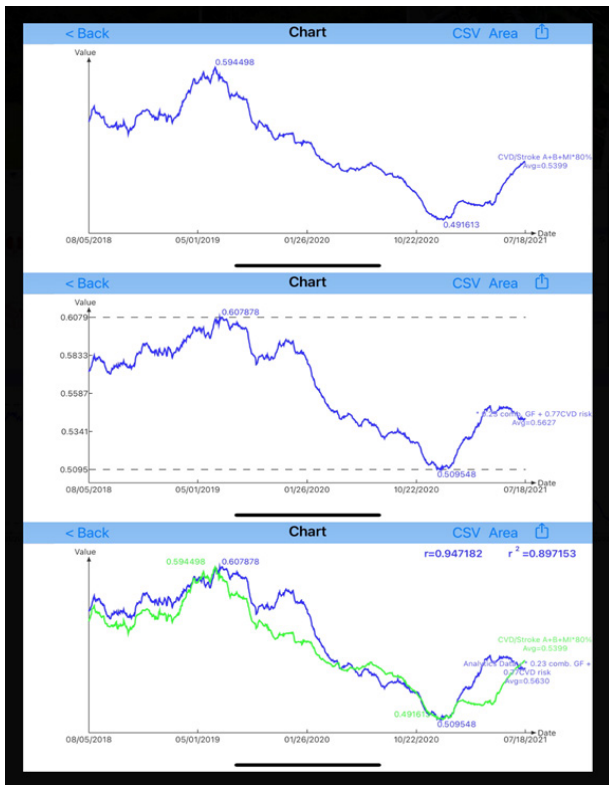


Figure 3: CVD risk curve using MI-only model and the 77% MI + 23% GF model

Figure 4 re-iterates the spirit and results from Figure 3 except that the author included quarterly results of 12-quarters (Q3Y18 - Q2Y21) in the upper diagram. The lower diagram in Figure 4 shows the 90-days moving average daily CVD risks using both MI-only model and MI+GF model. It is interesting to point out that *the average risk probabilities for the 12 quarters (54%) and the 1,170 days (56%) are almost identical with minor difference at the first decimal.* This finding is makes perfect sense since the quarterly data are calculated from the original daily data.

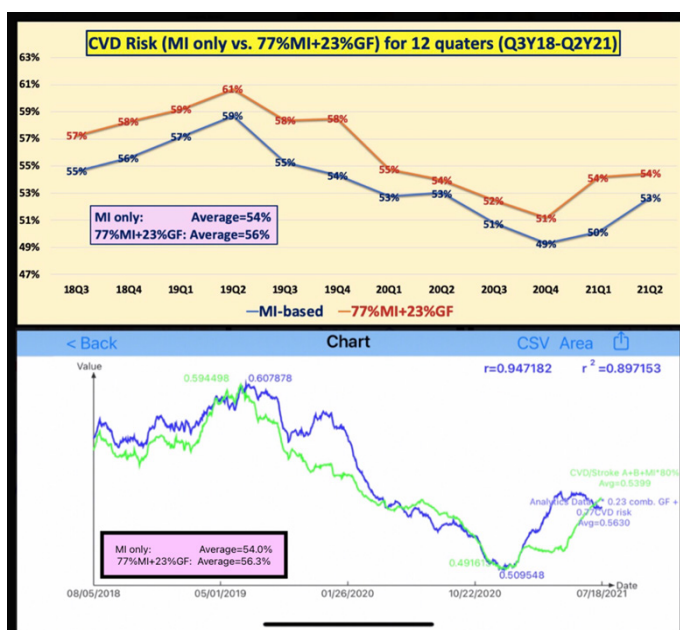


Figure 4: 12-quarters CVD risk curves and 1170-days CVD risk

curves using both MI-only and 77% MI + 23% GF model

Conclusions

In summary, the results from the comparison study between MI-only model (average risk level at 54%) and MI plus GF model (average risk level at 56.3%) is *a small CVD risk difference of 2% over this period of 1,170 days.* However, by further examining the daily diagram closely, some of the “local Risk deviations” are greater when the patient has more significant and larger amount of GF. This makes perfect biomedical and biophysical sense that a higher *GF is indeed associated with a higher amount of energy, where higher-energy can impact and damage internal vital organs such as the heart or brain.*

Based on the interesting findings from his research work regarding the file of GF and its impact, the author began focusing not only on his daily estimated HbA1C levels but also on the calculated GF magnitudes via CGM Glucose readings. Under the newly introduced element of GF into his iPhone APP, he has reached another level of his daily glycemic control for his type 2 diabetes.

References

For editing purposes, the majority of the references in this paper, which are self-references, have been removed for this article. Only references from other authors’ published sources remain. The bibliography of the author’s original self-references can be viewed at www.eclairermd.com.

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