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The GH-Method

Application of Estimated Energy Associated with Daily Glucose Fluctuations on Risk Assessment of Diabetes Complications, Especially the Risk Probability of Having a Cardiovascular Disease or Stroke Using GH-Method: Math-Physical Medicine (No. 431)

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Abstract

In this article, the author investigates the introduction of the glucose fluctuations (GF) factor into his CVD/stroke risk assessment method, physical and engineering modeling, and mathematical equation of calculating the risk probability of having severe diabetic complications, especially involving macro-blood vessels (arteries) related diseases, such as cardiovascular disease (CVD) or stroke. By integrating this extra influential factor of estimated energy associated GF via 3 different methods into his existing CVD risk assessment model using metabolism, his risk of having a stroke or CVD over the past 6 periods from 7/1/2018 and 4/9/2021 is increased by 4.6% (range from 3% to 7%). This conclusion comes from a direct comparison between the model without GF of 53.6% (range from 53%-58%) and 3 models applying 3 different energy estimation methods with GF of 58.2% (range from 53%-62%). His focus should be placed on the recent period from 1/1/2021 to 4/9/2021 because his risk of having a CVD or stroke is increased by 7%, from 50% without GF to 53% with GF (by method 2 and 3) or 57% (by Method 1). This discovery has proven that the incremental risk is completely due to higher GF during this short period. Although his risk calculation based on the metabolism model without GF is already at a low level of 50%, he did not pay any attention to his GF until very recently, in February of 2021. This discovery would send a strong warning message to him to keep his daily glucose waveform "as calm as possible" since the energy associated with bigger GF would cause additional threats of organ damage.

Keywords: Energy; Glucose; Diabetes; Cardiovascular disease; Stroke

Abbreviations: GF: glucose fluctuations; CVD: cardiovascular disease; MPM: math-physical medicine; MI: metabolism index; GHSU: general health status unit; HbA1C: hemoglobin A1c; CKD: chronic kidney disease; PPG: postprandial plasma glucose; CGM: continuous glucose monitoring; GV: glycemic variability; SMBG: self-monitored blood glucose; SD: standard deviation

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1. INTRODUCTION

The purpose of this article is to quantitatively demonstrate what type of changes would occur regarding his existing model and risk probability results of having a cardiovascular disease (CVD) or stroke by adding in a new influential factor, the glucose fluctuations (GF).

2. METHODS

2.1 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[1]. The second paper, No. 387 outlines the history of his personalized diabetes research, various application tools, and the differences between the biochemical medicine (BCM) approach vs. the MPM approach[2]. The third paper, No. 397 depicts a general flow diagram containing ~10 key MPM research methods and different tools[3].

2.2 CVD/stroke risk model based on metabolism

In 2014, the author applied the topology concept, finite-element engineering technique, and non-linear 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 (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), and pancreatic beta-cells self-recovering assessment. 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 interrelated.

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 CVD or stroke based on the patient's metabolic disorder conditions, unhealthy lifestyles, and the combined impact on the body.

2.3 The author's case of diabetes

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 average daily glucose of 250 mg/dL (HbA1C at 10%). During that year, his triglycerides reached 1161 (high risk for CVD and stroke) and the albumin-creatinine ratio (ACR) at 116 (high risk for CKD). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding the need for kidney dialysis treatment and the future high risk of dying from his severe diabetic complications.

In 2010, he decided to self-study endocrinology with an 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. By using his developed 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, dining 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, 4/10/2021, his weight was further reduced to ~165 lbs. (BMI 24.4) and his A1C was at 6.2% without any medication intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written 200 new research articles and published a total of 400 medical papers in various medical and engineering journals, but he has also achieved his best health conditions for the past 26 years. These achievements have resulted from his non-traveling, low-stress, and regular daily life routines. Of course, his in-depth knowledge of 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 the present day.

During the past 11 years, he has continuously investigated, studied, and analyzed his collected ~2 million data regarding his health status, medical conditions, and lifestyle details. He applies his knowledge, models, and tools from mathematics, physics, engineering, and computer science to conduct his medical research work. His entire medical research work is based on the aim of achieving high precision with quantitative proof in the biomedical findings, not just through linguistic expressions with qualitative words, vague statements, or complex medical terminologies.

His personal goal has been aiming at saving his own life through his research, and then helping his family members and other patients through distributing his knowledge learned and experiences gained from his 11-years medical research work to combat these chronic diseases and complications at the root cause level.

2.4 Other GV research work

There are many available articles regarding glycemic variability (GV), however, the author decides to include the following combined excerpt from two particular published articles[3-5]. These two 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. These papers focus on the comparison of many published GV articles and algorithm, method, and firmware design of a web-based app software for calculating GV values[3,4].

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 type 1 diabetes mellitus (T1DM) complications. In insulin-treated type 2 diabetes mellitus (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 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 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 optimal glycemic control over and above standard glycemic parameters, such as blood glucose and HbA1c. Avoiding both hyperglycemia and hypoglycemia by careful use of self-monitored blood glucose (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 GV 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 CVD 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 standard deviation (SD) is the most popular parameter for assessing GV 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 the use of GV 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 GV 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 reduce insulin resistance. This deterioration can be attributed to the progressive decline of ß-cell function. Even in subjects with well-controlled T2DM, 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 ß-cells and the vascular endothelium. Monnier et al. and Brownlee and Hirsch have recently emphasized that another component of dysglycemia, i.e., GV, 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 and the pancreatic ß-cell[3]."

2.5 Glucose fluctuations (GF)

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 general 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 SD from statistics. Although SD is widely used, it has limitations because the assumption of measured glucose data is normally distributed (similar to a Gaussian distribution), which is typically not the case. Besides, many research articles use glucose data collected within a few days from hospitalized patients rather than use glucose data collected over a few years from outpatients. The reason is that until recently after 2016-2017, the SMBG devices became available to diabetes out-patients to collect their own glucose data at home, instead of in the hospitals or clinic centers. However, the tasks of glucose data transfer from a CGM device to a computer and then the necessary follow-on tasks of data processing, data management, and data analysis still remain a challenge. 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 resulting in garbage outputs which fit the common expression in the computer science industry of "garbage in and garbage out".

Based on the above-mentioned theoretical and technical points, the author decided to conduct this study on applying the basic concept of GV (i.e., glucose fluctuation between peak and nadir) only, without using certain terms or formulas described in some of the publications. However, he 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 GF.

He re-named the GV as glucose fluctuations (GF) where GF equals 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 GV. The word variability can involve and signify many various things to different people.

GV can be applied to many clinical cases of greater mortality in intensive care, increased rate and risk of diabetes complications, and postprandial beta-cell dysfunction (insulin health)[6-8].

3. RESULTS

3.1 Collected input data

Since 5/5/2018, the author has been collecting 96 glucose data per day (every 15 minutes) and 288 glucose data per day (every 5 minutes) by using CGM. During the past 1,070 days (from 5/5/2018 to 4/9/2020), he has collected 308,160 glucose data (15-minute model).

For this study, he divided the big dataset into six half-year periods, except for the 6th period which contains 98 days only compared to the other 5 with 181-183 days per period. Therefore, in his energy calculation involving the horizontal axis of days or frequency components, he has to amplify the sixth period's results by a factor of (181/98 = 1.85) in order to have an equivalent energy estimation.

3.2 Three methods for estimated energy

The first method uses the square of Y-amplitude of GF (max-min of daily glucose) in the time domain.

The second method utilizes the Y-amplitude of the frequency domain.

The third method applies the Y-amplitude times the X-frequency components numbers to obtain the total area underneath the frequency curve in the frequency domain.

Method 2 and method 3 would produce almost identical results. Method 1 would generate a similar energy curve's shape (i.e., with extremely high correlation coefficients) but there is some degree of numerical differences with both method 2 and method 3.

After obtaining the estimated energy data, they need to be normalized by a factor of 0.735 which is the dividing break-even line in his developed metabolism model.

Finally, he uses 90% of the values calculated using the MI model without GF and 10% of the above-derived energy results using GF to add these two values together for his final results of CVD/stroke risk probability with the GF factor inside.

3.3 Graphic diagrams of results

Figure 1 shows the data table of input values and calculated results using three different methods to estimate the energy associated with GF.

Figure 2 depicts the calculated CVD risk diagram using 90% of the metabolism model and 10% of the GF energy model using method 1 (square of GF Y-magnitude in the time domain).

The risk of having a stroke or CVD over the past 6 periods between 7/1/2018 and 4/9/2021 is increased by 4.6% (range from 3% to 7%), based on a model applying metabolism without GF of 53.6% (range from 50%-58%) to a model employing metabolism with GF method 1 of 58.2% (range from 55%-61%). Method 1 uses the square of GF values in the time domain as the relative energy.

Figure 3 illustrates the CVD risk calculated diagram using 90% of metabolism model and 10% of GF energy using both method 2 (GF Y-magnitude in frequency domain) and method 3 (GF area underneath the GF curve in frequency domain).

The risk percentages and their resulted line charts are almost identical between method 2 and method 3. However, they still have some insignificant differences with the method 1 curve due to the different equations used. The risk of having a stroke or CVD over the past 6 periods from 7/1/2018 and 4/9/2021 is also increased by an identical 4.6% (range from 3% to 7%) in comparison to the metabolism

model without GF of an average of 53.6% (range from 50%-58%), and the two models (method 2 and method 3) using the metabolism model with GF of 58.2% (range from 53%-62%). Method 2 uses GF energy amplitude in FD values as the relative energy. Method 3 uses the GF area in FD.

CVD Risk with GF inputs (Energy 1)	2H18	1H19	2H19	1H20	2H20	1H21	Ideal Case
Avg Daily Glucose	*130*	*132*	*131*	*122*	*111*	*120*	120
Glucose Fluctuation (Max-Min)	*97*	*98*	*106*	*86*	*87*	*103*	80
Fluctuation / Glucose	75%	74%	81%	71%	78%	85%	67%
SQ of (Fluctuation/Glucose)	56%	55%	66%	50%	61%	72%	44%
Eneegy of Glucose (SQ of Gluc)	16999	17361	17069	14835	12248	14518	14400
Eneegy of Fluctuation (SQ of Fluc)	9493	9604	11232	7477	7529	10521	6400
Fluc Enegy /Glucose Energy	56%	55%	66%	50%	61%	72%	44%
(Period/Ideal) of (Fluc.E/Gluc.E) (Eneegy 1)	1.2565	1.2447	1.4805	1.1340	1.3831	1.6305	1.0000
Normalize to 0.735	0.923	0.915	1.088	0.834	1.017	1.198	0.735
10% of Normaized Fluc Eneegy	0.092	0.091	0.109	0.083	0.102	0.120	0.074
CVD Risk Probabilty %	*0.5512*	*0.5797*	*0.5505*	*0.5288*	*0.5037*	*0.5024*	
90% of CVD Risk	0.4961	0.5217	0.4955	0.4759	0.4533	0.4522	
10% Fluc Energy + 90% CVD Risk	0.5884	0.6132	0.6043	0.5593	0.5550	0.5720	
CVD Risk with GF inputs	2H18	1H19	2H19	1H20	2H20	1H21	Average
CVD Risk Changes	4%	3%	5%	3%	5%	7%	4.6%
CVD Risk without GF	55%	58%	55%	53%	50%	50%	53.6%
CVD Risk with GF	59%	61%	60%	56%	55%	57%	58.2%
CVD Risk with GF inputs (Energy 2)	2H18	1H19	2H19	1H20	2H20	1H21	Ideal Case
Avg Daily Glucose	*130*	*132*	*131*	*122*	*111*	*120*	120
Glucose Fluctuation (Max-Min)	*97*	*98*	*106*	*86*	*87*	*103*	80
Fluctuation / Glucose	75%	74%	81%	71%	78%	85%	67%
SQ of (Fluctuation/Glucose)	56%	55%	66%	50%	61%	72%	44%
FD-Y magnitude (GF Eneegy 2)	363	318	374	297	292	264	235
Normalize to 0.735	1.133	0.994	1.167	0.928	0.911	0.826	0.735
10% of Normaized Fluc Eneegy	0.113	0.099	0.117	0.093	0.091	0.083	0.074
CVD Risk Probabilty %	*0.5512*	*0.5797*	*0.5505*	*0.5288*	*0.5037*	*0.5024*	
90% of CVD Risk	0.4961	0.5217	0.4955	0.4759	0.4533	0.4522	
10% Fluc Energy + 90% CVD Risk	0.6094	0.6211	0.6122	0.5687	0.5445	0.5347	
CVD Risk Changes	6%	4%	6%	4%	4%	3%	4.6%
CVD Risk without GF	55%	58%	55%	53%	50%	50%	53.6%
CVD Risk with GF	61%	62%	61%	57%	54%	53%	58.2%
CVD Risk with GF inputs (Energy 3)	2H18	1H19	2H19	1H20	2H20	1H21	Ideal Case
Avg Daily Glucose	*130*	*132*	*131*	*122*	*111*	*120*	120
Glucose Fluctuation (Max-Min)	*97*	*98*	*106*	*86*	*87*	*103*	80
Fluctuation / Glucose	75%	74%	81%	71%	78%	85%	67%
SQ of (Fluctuation/Glucose)	56%	55%	66%	50%	61%	72%	44%
FD-Y magnitude (GF Eneegy 3)	66674	57284	68188	53912	53618	48252	42911
Normalize to 0.735	1.142	0.981	1.168	0.923	0.918	0.826	0.735
10% of Normaized Fluc Eneegy	0.114	0.098	0.117	0.092	0.092	0.083	0.074
CVD Risk Probabilty %	*0.5512*	*0.5797*	*0.5505*	*0.5288*	*0.5037*	*0.5024*	
90% of CVD Risk	0.4961	0.5217	0.4955	0.4759	0.4533	0.4522	
10% Fluc Energy + 90% CVD Risk	0.6103	0.6198	0.6122	0.5683	0.5452	0.5348	
CVD Risk Changes	6%	4%	6%	4%	4%	3%	4.6%
CVD Risk without GF	55%	58%	55%	53%	50%	50%	53.6%
CVD Risk with GF	61%	62%	61%	57%	55%	53%	58.2%
CVD Risk with GF inputs	2H18	1H19	2H19	1H20	2H20	1H21	Average
Risk without GF	55%	58%	55%	53%	50%	50%	53.6%
Risk with GF (Model 1)	59%	61%	60%	56%	55%	57%	58.2%
Risk with GF (Model 2)	61%	62%	61%	57%	54%	53%	58.2%
Risk with GF (Model 3)	61%	62%	61%	57%	55%	53%	58.2%
CVD Risk with GF inputs	2H18	1H19	2H19	1H20	2H20	1H21	Average
Risk Changes (Model 1)	4%	3%	5%	3%	5%	7%	4.6%
Risk Changes (Model 2)	6%	4%	6%	4%	4%	3%	4.6%
Risk Changes (Model 3)	6%	4%	6%	4%	4%	3%	4.6%

Figure 1: Data table of CVD risk with GF associated energy using three different GF energy methods.

4. CONCLUSION

In this article, the author investigates, through introducing the GF factor into his ready-developed CVD/stroke risk assessment method, physical and engineering modeling, and mathematical equation of calculating the risk probability of having severe diabetic complications, especially those macro-blood vessels (arteries) related diseases, such as stroke and CVD.

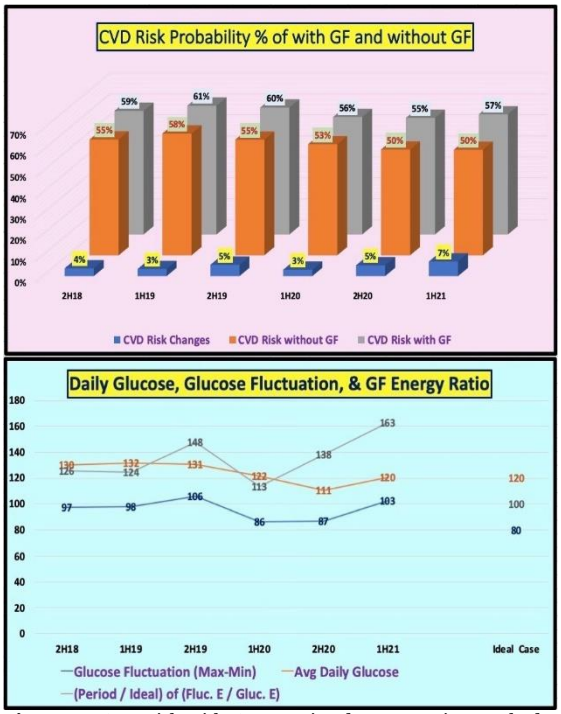

Figure 2: CVD risk with GF associated energy using method 1 (square of GF magnitude in TD).

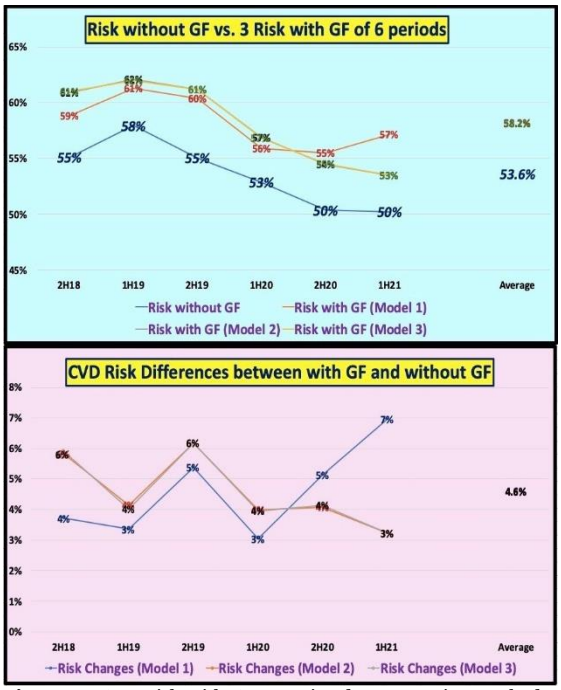

Figure 3: CVD risk with GF associated energy using method 1 (square of GF magnitude), method 2 (GF Y-amplitude in FD), and method 3 (GF curve's area in FD).

By introducing this extra influential factor of estimated energy associated with the GF via 3 different methods into his existing CVD risk assessment model using metabolism, his risk of having a stroke or CVD over the past 6 periods between 7/1/2018 and 4/9/2021 is increased by 4.6% (range from 3% to 7%). This conclusion comes from a direct comparison between the model without GF of

53.6% (range from 53%-58%) and 3 models applying 3 different energy estimation methods with GF of 58.2% (range from 53%-62%)[9,10].

He should personally pay special attention to the recent period from 1/1/2021 to 4/9/2021, his risk of having a CVD or stroke is increased by 7%, from 50% without GF to 53% with GF (by method 2 and 3) or 57% (by method 1). This discovery has proved that the incremental risk is completely due to higher GF during this short period[11-13]. Although his risk calculation based on the metabolism model without GF is already at a low level of 50%, however, he did not pay any attention to his GF situation until very recently, actually in February of 2021. This discovery would send a strong warning message to him to keep his daily glucose waveform "as calm as possible" since the energy associated with bigger GF would indeed bring in extra threat of his organ damage.

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