ISSN: 2640-4133

Research Article

Advances in Bioengineering & Biomedical Science Research

Continuous Glucose Monitoring Sensor Glucose Data Analysis of Time in Range, Time Above Range, Time Below Range and Waveform Comparison Study of Time in Range Curve Against both Average Daily Glucose Curve and Glucose Fluctuation Curve for a 3.3 Year Period based on GH-Method: Math-Physical Medicine (No. 500)

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Submitted: 06 Sep 2021; **Accepted:** 10 Sep 2021; **Published:** 28 Sep 2021

Citation: *Gerald C Hsu (2021) Continuous Glucose Monitoring Sensor Glucose Data Analysis of Time in Range, Time Above Range, Time Below Range and Waveform Comparison Study of Time in Range Curve Against both Average Daily Glucose Curve and Glucose Fluctuation Curve for a 3.3 Year Period based on GH-Method: Math-Physical Medicine (No. 500). Adv Bioeng Biomed Sci Res 4(3):106-110.*

Abstract

The author applies quantitative pattern and trend analysis tools using his collected continuous glucose monitoring (CGM) sensor data during a 3.3 year period from 5/8/2018 to 8/25/2021. Special attention has been placed on applying the American Diabetes Association (ADA) 2020 Guidelines for Time In Range (TIR) % with TIR average glucose values, Time Above Range (TAR) % with TAR average glucose value, and Time Below Range (TBR) % with TBR average glucose value. The purpose of this article is to study the correlations between the TIR curve and both average daily glucose curve (eAG) and glucose fluctuation curve (GF). GF is defined as the difference between the maximum glucose and the minimum glucose within one day or 24 hours duration. This GF term expresses the same meaning as the glycemic variability (GV) used by some diabetes research scientists. However, the author prefers GF over GV since GF describes the amplitude of glucose excursion in an exact and most direct way. Depending on the object of his research project, he sometimes selects the GF value within a meal's PPG waveform of a 3-hours duration.

Furthermore, ***the "primary range" of TIR is defined between 70 mg/dL and 180 mg/dL while a "secondary range" of TIR is defined between 70 mg/dL and 140 mg/dL.*** *Of course, both the TIR's and TAR's percentages and their averaged values of secondary range (difference of 70 mg/dL) are smaller than the primary range results due to the secondary range's narrower glucose range of 40 mg/dL (110-70 or 180-140).*

In summary, there are five noticeable findings from this study:

(1) TIR: His TIR percentage (89%) and average TIR value (121 mg/dL) of the primary range, along with the TIR percentage (72%) and average TBR value (114 mg/dL) of the secondary range represent the ***majority*** *of the data. This means that* ***his type 2 diabetes (T2D) is quite well under control.***

(2) TBR: His TBR percentage (5%) and average TBR value (65 mg/dL) of the primary range, along with the same TBR percentage (5%) and the same average TBR value (65 mg/dL) of the secondary range contain rather ***small amounts****. This means that* ***his risk of having hypoglycemia (insulin shock) is relatively low.***

(3) TAR: His TAR percentage (6%) and average TAR value (194 mg/dL) of the primary range have a lower percentage but a higher averaged glucose value than the TAR percentage (23%) and average TBR value (158 mg/dL) of the secondary range. However, the higher TAR percentage (23%) and its associated lower averaged TBR value (158 mg/dL) of the secondary range show that ***his T2D's hyperglycemia control still has room (specifically between 140 mg/dL and 180 mg/dL) for improvement.***
(4) T2D: The existence with occasional glucose levels of being greater than 180 mg/dL or below 70 mg/dL confirms that he

still is a "T2D patient" regardless of his diabetes conditions being well under controlled since 2017.

(5) Correlation coefficients: First of all, his eAG and GF have a strong correlation of +69%. This means that ***when his eAG is high, then most likely GF is also*** *high. Secondly, his eAG and TIR have a correlation of -79% (negatively high) and GF and TIR have an even stronger correlation of -89% (negatively higher). These two results of very high negative correlations indicate that* ***when both eAG and GF are higher, his TIR would be lower, and vice versa.***

Introduction

The author applies quantitative pattern and trend analysis tools using his collected continuous glucose monitoring (CGM) sensor data during a 3.3 year period from 5/8/2018 to 8/25/2021. Special attention has been placed on applying the American Diabetes Association (ADA) 2020 Guidelines for Time In Range (TIR) % with TIR average glucose values, Time Above Range (TAR) % with TAR average glucose value, and Time Below Range (TBR) % with TBR average glucose value. The purpose of this article is to study the correlations between the TIR curve and both average daily glucose curve (eAG) and glucose fluctuation curve (GF). GF is defined as the difference between the maximum glucose and the minimum glucose within one day or 24 hours duration. This GF term expresses the same meaning as the glycemic variability (GV) used by some diabetes research scientists. However, the author prefers GF over GV since GF describes the amplitude of glucose excursion in an exact and most direct way. Depending on the object of his research project, he sometimes selects the GF value within a meal's PPG waveform of a 3-hours duration.

Furthermore, ***the "primary range" of TIR is defined between 70 mg/dL and 180 mg/dL while a "secondary range" of TIR is defined between 70 mg/dL and 140 mg/dL***. Of course, both the TIR's and TAR's percentages and their averaged values of secondary range (difference of 70 mg/dL) are smaller than the primary range results due to the secondary range's narrower glucose range of 40 mg/dL (110-70 or 180-140).

Methods

MPM Background

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

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.

All of listed papers in the section of references are from his written and published medical research articles.

The Author'S Case of Diabetes and Complications

The author has been a severe T2D patient since 1996. He weighed 220 lb. (100 kg, BMI 32.5) at that time. By 2010, he still weighed 198 lb. (BMI 29.2) with an average daily glucose of 250 mg/dL (HbA1C of 10%). During that year, his triglycerides reached to 1161 (diabetic retinopathy, DR) and albumin-creatinine ratio (ACR) at 116 (chronic kidney diseases, CKD). He also suffered from five cardiac episodes within a decade. In 2010, three independent physicians warned him regarding his needs of kidney dialysis treatment and his future high risk of dying from his severe diabetic complications. Other than cerebrovascular disease (stroke), he has suffered most of known diabetic complications, including both macro-vascular and micro-vascular complications.

In 2010, he decided to launch his self-study on endocrinology, diabetes, and food nutrition in order to save his own life. During 2015 and 2016, he developed four prediction models related to diabetes conditions: weight, postprandial plasma glucose (PPG), fasting plasma glucose (FPG), and A1C. As a result, from using his developed mathematical metabolism index (MI) model in 2014 and the four prediction tools, by end of 2016, his weight was reduced from 220 lbs. (100 kg, BMI 32.5) to 176 lbs. (89 kg, BMI 26.0), waistline from 44 inches (112 cm, nonalcoholic fatty liver disease /NAFLD) to 33 inches (84 cm), average finger glucose reading from 250 mg/dL to 120 mg/dL, and lab-tested A1C from 10% to ~6.5%. One of his major accomplishments is that *he no longer takes any diabetes medications since 12/8/2015*.

In 2017, he has achieved excellent results on all fronts, especially his glucose control. However, during the pre-COVID period of 2018 and 2019, he traveled to approximately 50+ international cities to attend 65+ medical conferences and made ~120 oral presentations. This hectic schedule inflicted damage to his diabetes control, through dinning out frequently, post-meal exercise disruption, jet lag, and along with the overall metabolism impact due to his irregular life patterns through a busy travel schedule; therefore, his glucose control and overall metabolism state were somewhat affected during this two-year heavier traveling period.

During 2020 with a COVID-19 quarantined lifestyle, not only has he published ~400 medical papers in 100+ journals, but he has also reached his best health conditions for the past 26 years. By the beginning of 2021, his weight was further reduced to 165 lbs. (BMI 24.4) along with a 6.1% A1C value (daily average glucose at 105 mg/dL), without having any medication interventions or insulin injections. These good results are due to his non-traveling, low-stress, and regular daily life routines. Due to his knowledge of chronic diseases, practical lifestyle management experiences, and developed various high-tech tools contribute to his excellent health status since 1/19/2020, which is the start date of being self-quarantined.

On 5/5/2018, he applied a CGM sensor device on his upper arm and checks glucose measurements every 5 minutes for a total of ~288 times each day. He has maintained the same measurement pattern to present day. In his research work, he uses the CGM sensor glucose at time-interval of 15 minutes (96 data per day). By the way, the difference of average sensor glucoses between 5-minute intervals and 15-minute intervals is only 0.4% (*average glucose of 114.81 mg/dL for 5-minutes and average glucose of 114.35 mg/dL for 15-minutes with a correlation of 93% between these two sensor glucose curves*) during the period from

2/19/20- to 8/13/21.

Therefore, over the past 11 years, he could study and analyze the 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 medical research work is based on the aims of achieving both "high precision" with "quantitative proof" in the medical findings.

The following timetable provides a rough sketch of the emphasis of his medical research during each stage:

- 2000-2013: Self-study diabetes and food nutrition, developing a data collection and analysis software.
- 2014: Develop a mathematical model of metabolism, using engineering modeling and advanced mathematics.
- 2015: Weight & FPG prediction models, using neuroscience.
- 2016: PPG & HbA1C prediction models, using optical physics, artificial intelligence (AI), and neuroscience.
- 2017: Complications due to macro-vascular research such as CVD, coronary heart disease (CHD) and stroke, using pattern analysis and segmentation analysis.
- 2018: Complications due to micro-vascular research such as CKD, bladder, foot, and eye issues (DR).
- 2019: CGM big data analysis, using wave theory, energy theory, frequency domain analysis, quantum mechanics, and AI.
- 2020: Cancer, dementia, longevity, geriatrics, DR, hypothyroidism, diabetic foot, diabetic fungal infection, and linkage between metabolism and immunity, learning about certain infectious diseases, such as COVID-19.
- 2021: Applications of linear elastic glucose theory (LEGT) and perturbation theory from quantum mechanics on medical research subjects, such as chronic diseases and their complications, cancer, and dementia. Using metabolism and immunity.it's as the base, he expands his research into cancers, semantic, and COVID-19.

Again, to date, he has collected more than two million data regarding his medical conditions and lifestyle details. In addition, he has written 498 medical papers and published 400+ articles in 100+ various medical journals, including 6 special editions with his 20-25 papers exclusively for each edition. Moreover, he has given ~120 presentations at ~65 international medical conferences. He has continuously dedicated time and effort on medical research work and shared his findings and learnings with other patients worldwide.

ADA TIR% Guidelines

In February 2019, the Advanced Technologies & Treatments for Diabetes (ATTD) Congress assembled an international panel of individuals with diabetes and clinicians and researchers with expertise in CGM. Their objective was to develop clinical CGM targets to supplement the currently agreed-upon metrics for CGM-derived times in three glucose ranges (within TIR, TBR, and TAR) in order to provide guidance for clinicians, researchers, and individuals with diabetes in using, interpreting, and reporting CGM data in routine clinical care and research.

Recently in 2020, the ADA published revised guidelines regarding the CGM collected data which included three newly recommended measurement guidelines: (1) TIR: 70-180 mg/dL for "acceptable" diabetes glucose range; (2) TAR: >180 mg/dL for severe diabetes concerns; and (3) TBR: <70 mg/dL as a warning for insulin shock.

Although the author has already made noticeable improvements on his diabetes control, he wanted to achieve better conditions. Therefore, he established another set of guidelines for his more stringent glucose control by replacing the 180 mg/dL cutoff line with a lower 140 mg/dL for both TIR and TAR. As described above regarding his T2D history, eAG was higher (above 140 mg/dL) prior to 2015 and gradually trended downward around or less than 120 mg/dL after 2017. ***Therefore, he adopts two TIR ranges in this particular study, both the primary range of 70-180 mg/dL and the secondary range of 70-140 mg/dL.***

After the ADA's announcement, several research papers have been written regarding this subject. Some minor data differences exist in the studies between References 4 and 5; however, these research papers are based on collected CGM data belonging to diabetes patients. Lacking clear evidence, the author would like to make a logical assumption that "most" of the tested data collected from patients were taking medications. As we know, ***medications have a strong, obvious, and significant effect on suppressing the external symptom of diabetes, but they are not fixing the root causes of the disease.*** As of 12/8/2015, he has discontinued all of his diabetes medications; therefore, ***his glucose results are derived directly from his body's biomedical conditions without external chemical interventions***.

Results

Figure 1 shows the primary range and secondary range ***of percentages*** for TIR, TAR, and TBR.

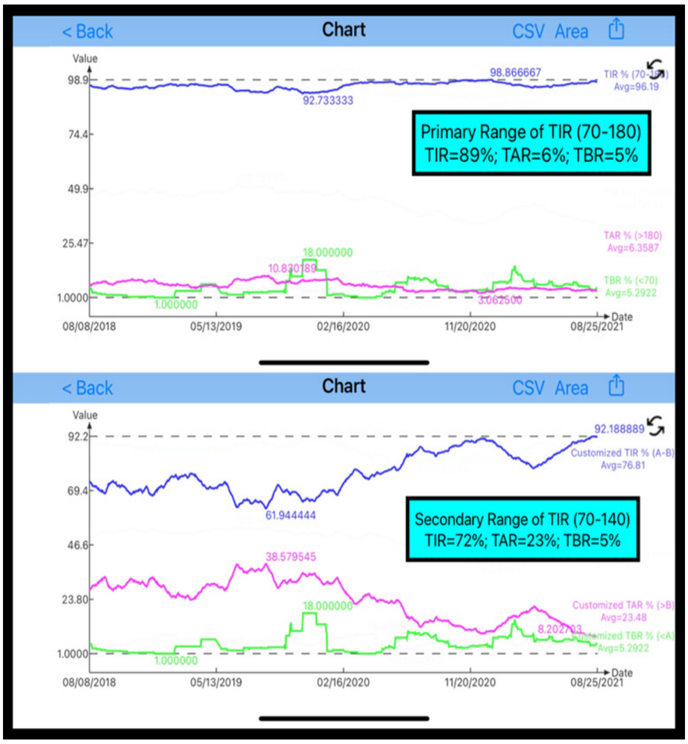

Figure 1: 90-days moving average curves of TIR, TAR, and TBR percentage (5/5/2018 - 8/25/2021)

Figure 2 depicts the primary range and secondary range of ***averaged glucose values*** for TIR, TAR, and TBR.

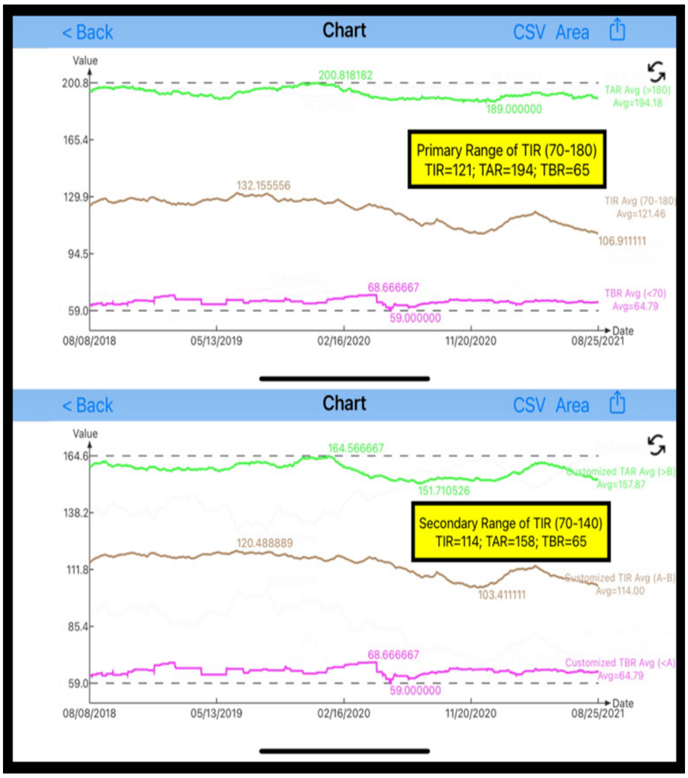

Figure 2: 90-days moving average curve of TIR, TAR, and TBR glucose value (5/5/2018 - 8/25/2021)

The following table lists the summarized data of Figure 1 and Figure 2:

Primary Range (180 mg/dL):
TIR % & avg. glucose: (89%, 121)
TAR % & avg. glucose: (6%, 194)
TBR % & avg. glucose: (5%, 65)

Secondary Range (140 mg/dL):
TIR % & avg. glucose: (72%, 114)
TAR % & avg. glucose: (23%, 158)
TBR % & avg. glucose: (5%, 65)

Figure 3 is a byproduct of data pattern and trend representation of this special analysis for TIR, TBR, and TAR. He illustrates his calculated correlation coefficients among TIR curve, eAG curve, and GF curve. These correlations are demonstrating the inter-relationships of the three primary indexes of diabetes.

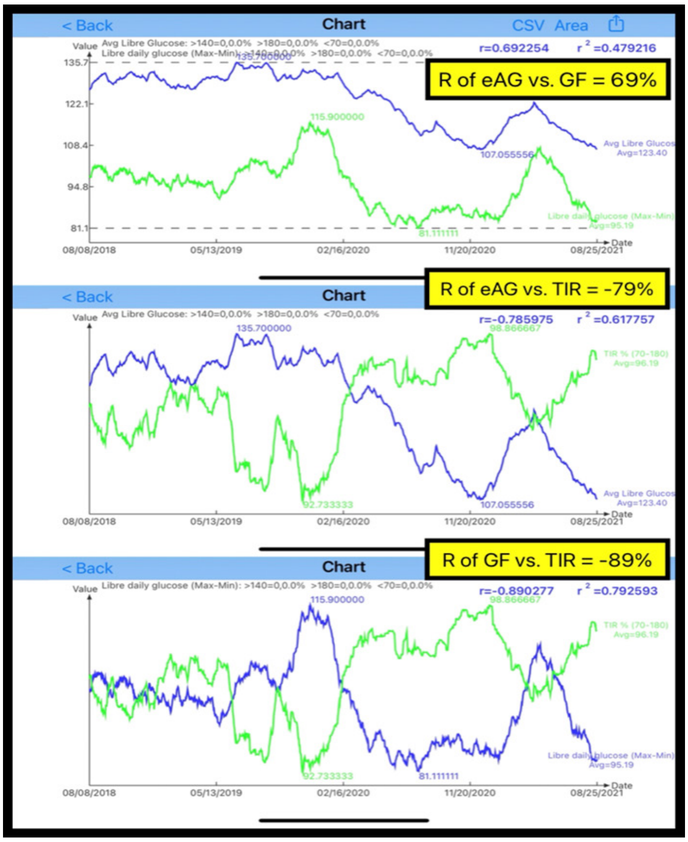

Figure 3: Correlations among TIR, eAG, and GF (90-days moving average curves)

From Figure 3, ***his eAG and GF have a strong correlation of +69%. This means that when his eAG is high, then most likely GF is also high***. Furthermore, his eAG and TIR have a correlation of -79% (negatively high) and ***GF and TIR have an even stronger correlation of -89%*** (negatively higher). These two results of very high negative correlations indicate that when both eAG and GF are higher, his TIR would be lower, and vice versa.

Conclusions

In summary, there are five noticeable findings from this study:

1. TIR: His TIR percentage (89%) and average TIR value (121 mg/dL) of the primary range, along with the TIR percentage (72%) and average TBR value (114 mg/dL) of the secondary range represent the majority of the data. This means that ***his type 2 diabetes (T2D) is quite well under control.***

2. TBR: His TBR percentage (5%) and average TBR value (65 mg/dL) of the primary range, along with the same TBR percentage (5%) and the same average TBR value (65 mg/dL) of the secondary range contain ***rather small amounts***. This means that ***his risk of having hypoglycemia (insulin shock) is relatively low.***
3. TAR: His TAR percentage (6%) and average TAR value (194 mg/dL) of the primary range have a lower percentage but a higher averaged glucose value than the TAR percentage (23%) and average TBR value (158 mg/dL) of the secondary range. However, the higher TAR percentage (23%) and its associated lower averaged TBR value (158 mg/dL) of the secondary range show that ***his T2D's hyperglycemia control still has room (specifically between 140 mg/dL and 180 mg/dL) for improvement.***
4. T2D: The existence with occasional glucose levels of being greater than 180 mg/dL or below 70 mg/dL confirms that he still is a "T2D patient" regardless of his diabetes conditions being well under controlled since 2017.
5. Correlation coefficients: First of all, his eAG and GF have a strong correlation of +69%. This means that when his eAG is high, then most likely GF is also high. Secondly, his ***eAG and TIR have a correlation of -79%*** (negatively high) and GF and TIR have an even stronger correlation of -89% (negatively higher). These two results of very high negative correlations indicate that ***when both eAG and GF are higher, his TIR would be lower, and vice versa.***

References

For editing purposes, 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.eclairemd.com.

Readers may use this article as long as the work is properly cited, and their use is educational and not for profit, and the author's original work is not altered.

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