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Research Article

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The relationship between diabetic retinopathy and hypothyroidism and time-in-range percentages of glucoses using the viscoplastic energy model of GH-Method: math-physical medicine (No. 951, VMT #350, 11/12/2023)

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Abstract

Upon reviewing a PubMed article (referenced in this paper's section of introduction) comparing diabetic retinopathy (DR) conditions and hypothyroidism (elevated TSH) with glucose time-in-range percentages, the author was intrigued about applying a different research method, the space-domain Viscoplastic Medicine model (SD-VMT) alongside traditional statistical correlations to his own collected data.

For this investigation, the author utilized six years of personal data obtained through a Libre brand continuous glucose monitoring (CGM) device from 5/1/2018 to 11/11/2023. To maximize data utilization, the author estimated Time in Range (TIR) for 2017. Despite this being an estimate, the author believes it won't significantly distort conclusions due to the SD-VMT method's initialization process.

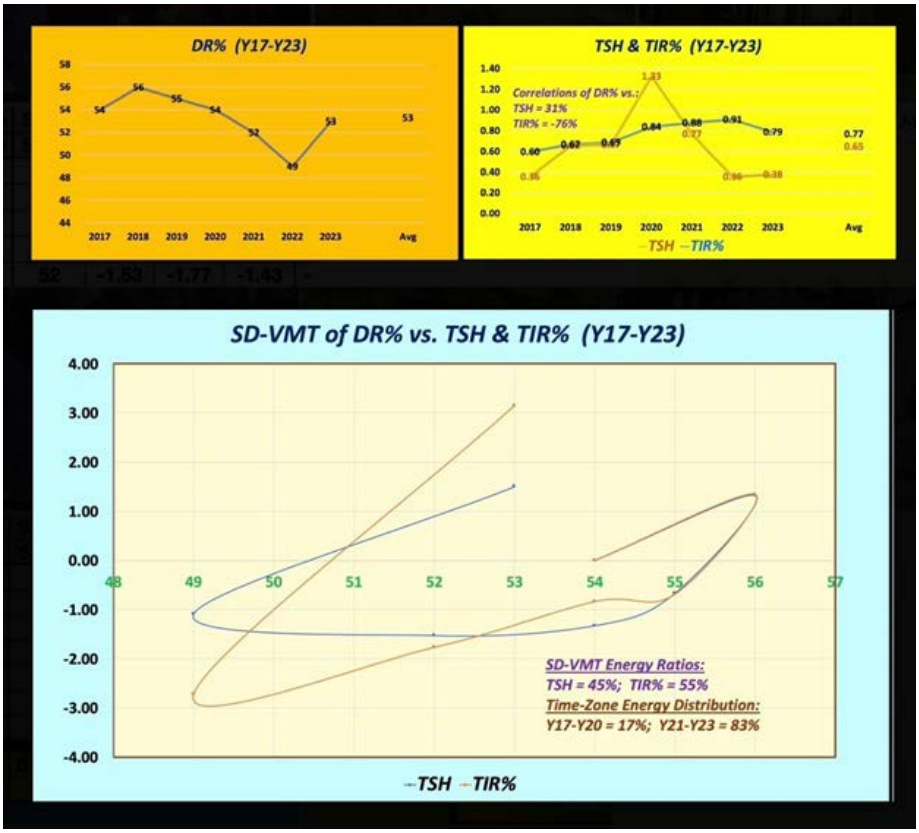
***In summary,** employing traditional statistical correlation, the author noted a low correlation (31%) between his risks of diabetic retinopathy (DR) and his thyroid TSH values. However, a high negative correlation of -76% was found between his DR risk and his TIR % of glucoses, indicating that higher TIR associates with lower DR risk, aligning with the author's expectations.*

- ***DR and TSH (hypothyroidism): 31%***
- ***DR and TIR (type 2 diabetes): -76%***

Using a space-domain Viscoplastic Energy Analysis (SD-VMT), the author derived two close contribution margins, but with a noticeable 10% numerical difference on contribution:

- ***TSH thyroid energy: 45%***
- ***TIR Glucose energy: 55%***

These two contribution ratios imply that TIR in type 2 diabetes glucose condition primarily contributes to the risk of diabetic retinopathy, while TSH in the thyroid condition is a secondary contributor to the risk of DR.



1. Introduction

Upon reviewing a PubMed article (referenced in this paper's section of introduction) comparing diabetic retinopathy (DR) conditions and hypothyroidism (elevated TSH) with glucose time-in-range percentages, the author was intrigued about applying a different research method, the space-domain Viscoplastic Medicine model (SD-VMT) alongside traditional statistical correlations to his own collected data.

For this investigation, the author utilized six years of personal data obtained through a Libre brand continuous glucose monitoring (CGM) device from 5/1/2018 to 11/11/2023. To maximize data utilization, the author estimated Time in Range (TIR) for 2017. Despite this being an estimate, the author believes it won't significantly distort conclusions due to the SD-VMT method's initialization process.

1.1. Biomedical information

The following sections contain excerpts and concise information drawn from multiple medical articles, which have been meticulously reviewed by the author of this paper. The author has adopted this approach as an alternative to including a conventional reference list at the end of this document, with the intention of optimizing his valuable research time. It is essential to clarify that these sections do not constitute part of the author's original contribution but have been included to aid the author in his future reviews and offer valuable insights to other readers with an interest in these subjects.

1.2. Pathophysiological explanations of relationship between diabetic retinopathy (DR) and hypothyroidism

There isn't a well-established direct pathophysiological relationship between diabetic retinopathy and hypothyroidism. But, both conditions can have systemic effects on various organs, and some indirect connections may exist. Here are some considerations for each condition:

Diabetic Retinopathy:

1. Microvascular Damage: Diabetic retinopathy primarily involves microvascular damage in the retina due to chronic high blood sugar levels.

2. Ischemia & Neovascularization: This damage can lead to ischemia (reduced blood supply) in the retina, prompting neovascularization (abnormal blood vessel growth) as a compensatory response.

Hypothyroidism:

1. Metabolic Slowdown: Hypothyroidism involves a reduced production of thyroid hormones, leading to a slowdown in various metabolic processes throughout the body.

2. Cardiovascular Effects:

Hypothyroidism can impact cardiovascular function, potentially affecting blood supply to various organs, including the eyes.

While both conditions can have vascular implications, and disruptions in blood supply are a common theme, ***a direct causative link between diabetic retinopathy and hypothyroidism hasn't been firmly established in the literature.*** It's important to approach these conditions separately and manage them based on their respective underlying causes.

Nevertheless, ***diabetic retinopathy and hypothyroidism are two distinct medical conditions with different pathophysiological explanations.***

Diabetic Retinopathy:

1. Microvascular Damage: Chronic high blood sugar levels in diabetes can damage the small blood vessels in the retina, leading to microvascular changes.

2. Ischemia and Hypoxia: The damaged blood vessels may result in ***reduced blood supply (ischemia)*** and ***inadequate oxygen delivery (hypoxia)*** to the retinal tissues.

3. Neovascularization: As a response to ischemia, abnormal new blood vessels may form, which are fragile and prone to leakage, contributing to vision complications.

4. Inflammation and Increased Permeability: Inflammatory processes and increased permeability of blood vessels can further exacerbate retinal damage.

Hypothyroidism:

1. Reduced Thyroid Hormone Production: Hypothyroidism is characterized by an insufficient production of thyroid hormones (T3 and T4) by the thyroid gland.

2. Metabolic Slowdown: Thyroid hormones play a crucial role in regulating metabolism. Reduced levels lead to a slowdown in various metabolic processes throughout the body.

3. Changes in Tissue Function: Hypothyroidism affects nearly every organ system, including the eyes. Dry eyes and changes in the function of the eye muscles can occur.

4. Myxedema: Severe hypothyroidism may lead to myxedema, a condition where the tissues retain fluid, causing puffiness around the eyes and affecting the facial appearance.

5. Cardiovascular Changes: Hypothyroidism can lead to changes in lipid profiles and cardiovascular function, potentially impacting the blood supply to various organs, including the eyes.

It's important to note that both conditions involve complex interactions and can have systemic effects beyond their primary target organs. Management typically involves addressing the underlying causes, such as blood sugar control in diabetes and thyroid hormone replacement therapy in hypothyroidism.

1.3. Pathophysiological explanations of relationship between diabetic retinopathy (DR) and time in range (TIR) of glucoses

The relationship between diabetic retinopathy (DR) and time in range (TIR) of glucose levels involves the impact of glycemic control on the development and progression of retinal complications. Here's a simplified overview:

1. Chronic Hyperglycemia: Persistent high blood glucose levels (hyperglycemia) contribute to the development of diabetic retinopathy. The longer the duration of elevated glucose, the higher the risk of retinal complications.

2. Endothelial Damage: Prolonged exposure to high glucose levels can cause damage to the endothelial cells lining the blood vessels, including those in the retina.

3. Microvascular Changes: Diabetic retinopathy is characterized by microvascular changes, such as weakened and leaky blood vessels in the retina. These changes are influenced by the cumulative impact of glucose fluctuations over time.

4. Impact of Time in Range (TIR): TIR represents the percentage of time spent within a target glucose range, e.g. between 70 mg/dL and 180 mg/dL. Maintaining glucose levels within a recommended range, rather than experiencing extreme highs and lows, can help mitigate the damaging effects of hyperglycemia on the retinal vasculature.

5. Prevention of Glycemic Extremes: Consistent TIR within the target range is associated with a lower risk of diabetic complications, including retinopathy. Minimizing the time spent in hyperglycemia (r.g. greater than 180 mg/dL) or hypoglycemia (e.g. less than 70 mg/dL) helps prevent or slow the progression of microvascular complications.

6. Individualized Glycemic Targets: The ideal TIR may vary among individuals, and healthcare professionals often set personalized glycemic targets based on factors such as age, health status, and the presence of complications like diabetic retinopathy.

In summary, maintaining a higher TIR within a recommended glucose range is generally associated with better outcomes in terms of preventing and managing diabetic retinopathy. Regular monitoring of blood glucose levels and adherence to a diabetes management plan are essential components of preventing or slowing the progression of diabetic retinopathy.

Thyroid stimulating hormone (TSH)

Normal values of thyroid-stimulating hormone (TSH) are from ***0.4 to 4.0 mIU/L*** for those with no symptoms of an under- or over-active thyroid. For example, when TSH value is 5.0 generally indicate hypothyroidism rather than hyperthyroidism.

TSH is produced by the pituitary gland and helps regulate the production of thyroid hormones by the thyroid gland. In hypothyroidism, the thyroid gland is underactive and produces insufficient amounts of thyroid hormones, resulting in elevated TSH levels as the pituitary gland attempts to stimulate the thyroid gland to produce more hormones.

Conversely, in hyperthyroidism, the thyroid gland is overactive and produces excessive amounts of thyroid hormones, leading to decreased TSH levels as the pituitary gland reduces its production to try to regulate the thyroid hormones.

1.4. Pathophysiological explanations of relationships between hypothyroidism (high TSH) and ACR of kidney biomarker

The relationship between hypothyroidism (elevated TSH) and increased albumin-to-creatinine ratio (ACR), a kidney biomarker, may involve impaired renal function due to altered hemodynamics, inflammation, and oxidative stress associated with hypothyroidism. Additionally, hypothyroidism can lead to changes in vascular permeability, potentially contributing to elevated ACR. However, the exact pathophysiological mechanisms are complex and may vary among individuals.

1.5. Pathophysiological explanations of relationships between hypothyroidism (high TSH) and glucose (HbA1C) of type 2 diabetes

The relationship between hypothyroidism (elevated TSH) and glucose control, as measured by HbA1c in type 2 diabetes, can be attributed to various factors. Hypothyroidism may lead to insulin resistance, impair insulin secretion, and disrupt glucose metabolism. Additionally, it can contribute to weight gain and alterations in lipid profiles, further exacerbating insulin resistance. These interconnected mechanisms can collectively

contribute to poor glycemic control and higher HbA1c levels in individuals with both hypothyroidism and type 2 diabetes. It is important to note that the impact can vary among individuals.

1.6. The excerpt of a PubMed report

Association of thyroid stimulating hormone (TSH) and time in range (TIR) with risk of diabetic retinopathy (DR) in euthyroid type 2 diabetes (T2D)

By: Yaxin Wang et al.

Diabetes Metab Res Rev. September of 2023 ***Abstract***

Aims:

Diabetic retinopathy (DR) can occur even in well-controlled type 2 diabetes, suggesting residual risks of DR in this population. In particular, we investigated the combined effect of thyroid function and glycaemic control assessed by an emerging metric, time in range (TIR) with DR.

Materials and methods:

In this cross-sectional study, a total of 2740 euthyroid patients with type 2 diabetes were included. Thyroid indicators, including thyroidstimulating hormone (TSH), free triiodothyronine, free thyroxine, thyroid peroxidase antibody and thyroglobulin antibody, were measured. TIR was measured using continuous glucose monitoring data.

Results:

Overall, the multivariable-adjusted odds ratios (ORs) for DR across ascending tertiles of TSH were 1.00 (reference), 1.06 (95% confidence interval [CI] 0.85-1.32), and 1.48 (95% CI 1.19-1.85). Even in wellcontrolled participants who achieved a TIR target of >70% (n = 1449), the prevalence of DR was 23.8%, which was significantly related to TSH (OR = 1.54, 95% CI 1.12-2.12, highest vs. lowest TSH tertile). Participants were then classified into 6 groups by the joint categories of TIR (>70%, ≤70%) and TSH (tertiles), and the multivariable-adjusted ORs for DR were highest in TIR ≤70% and the highest TSH tertile group (OR = 1.96, 95% CI 1.41-2.71) when compared with the TIR >70% and the lowest TSH tertile group.

Conclusions:

In type 2 diabetic patients with wellcontrolled glycaemic status, higher TSH within the normal range was associated with an increased risk of DR. The combination of suboptimal TSH and TIR further increased the risk of DR.

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 his published 760+ papers.

The first paper, No. 386 (Reference 1) describes his MPM methodology in a general conceptual format. The second paper, No. 387 (Reference 2) 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 (Reference 3) depicts a general flow diagram containing ~10 key MPM research methods and different tools.

The author's diabetes history: The author was a severe T2D patient since 1995. 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 1161 (high risk for CVD and stroke) and his 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 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. He spent the entire year of 2014 to develop a metabolism index (MI) mathematical model. During 2015 and 2016, he developed four mathematical prediction models related to diabetes conditions: weight, PPG, fasting plasma glucose (FPG), and HbA1C (A1C). Through using his developed mathematical metabolism index (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 fingerpiercing 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 achieved excellent results on all fronts, especially his glucose control. However, during the preCOVID 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, and 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 COVID-19 selfquarantined life on 1/19/2020. By 10/16/2022, his weight was further reduced to ~164 lbs. (BMI 24.22) and his A1C was at 6.0% without any medication intervention or insulin injection. In fact, with the special COVID-19 quarantine lifestyle since early 2020, not only has he written and published ~500 new research articles in various medical and engineering journals, but he has also achieved his best health conditions for the past 27 years. These achievements have resulted from his non-traveling, low-stress, and regular daily life routines. Of course, his indepth 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. Furthermore, he extracted the 5minute intervals from every 15minute interval for a total of 96 glucose data each day stored in his computer software.

Through the author's medical research work over 40,000 hours and read over 4,000 published medical papers online in the past 13 years, he discovered and became convinced that good life habits of not smoking, moderate or no alcohol intake, avoiding illicit drugs; along with eating the right food with wellbalanced nutrition, persistent exercise, having a sufficient and good quality of sleep, reducing all kinds of unnecessary stress, maintaining a regular daily life routine contribute to the risk reduction of having many diseases, including CVD, stroke, kidney problems, micro blood vessels issues, peripheral nervous system problems, and even cancers and dementia. In addition, a long-term healthy lifestyle can even "repair" some damaged internal organs, with different required time-length depending on the particular organ's cell lifespan. For example, he has "self-repaired" about 35% of his damaged pancreatic beta cells during the past 10 years.

1.7. Energy theory

The human body and organs have around 37 trillion live cells which are composed of different organic cells that require energy infusion from glucose carried by red blood cells; and energy consumption from laborwork or exercise. When the residual energy (resulting from the plastic glucose scenario) is stored inside our bodies, it will cause different degrees of damage or influence to many of our internal organs.

According to physics, energies associated with the glucose waves are proportional to the square of the glucose amplitude. The residual energies from elevated glucoses are circulating inside the body via blood vessels which then impact all of the internal organs to cause different degrees of damage or influence, e.g. diabetic complications. Elevated glucose (hyperglycemia) causes damage to the structural integrity of blood vessels. When it combines with both hypertension (rupture of arteries) and hyperlipidemia (blockage of arteries), CVD or Stroke happens. Similarly, many other deadly diseases could result from these excessive energies which would finally shorten our lifespan. For an example, the combination of hyperglycemia and hypertension would cause micro-blood vessel's leakage in kidney systems which is one of the major cause of CKD.

The author then applied Fast Fourier Transform (FFT) operations to convert the input wave from a time domain into a frequency domain. The y-axis amplitude values in the frequency domain indicate the proportional energy levels associated with each different frequency component of input occurrence. ***Both output symptom value (i.e. strain amplitude in the time domain) and output symptom fluctuation rate (i.e. the strain rate and strain frequency) are influencing the energy level (i.e. the Y-amplitude in the frequency domain).***

Currently, many people live a sedentary lifestyle and lack sufficient exercise to burn off the energy influx which causes them to become overweight or obese. Being overweight and having obesity leads to a variety of chronic diseases, particularly diabetes. In addition, many types of processed food add unnecessary ingredients and harmful chemicals that are toxic to the bodies, which lead to the development of many other deadly diseases, such as cancers. For example, ~85% of worldwide diabetes patients are overweight, and ~75% of patients with cardiac illnesses or surgeries have diabetes conditions.

In engineering analysis, when the load is applied to the structure, it bends or twists, i.e. deform; however, when the load is removed, it will either be restored to its original shape (i.e, elastic case) or remain in a deformed shape (i.e. plastic case). In a biomedical system, the glucose level will increase after eating carbohydrates or sugar from food; therefore, the carbohydrates and sugar function as the energy supply. After having labor work or exercise, the glucose level will decrease. As a result, the exercise burns off the energy, which is similar to load removal in the engineering case. In the biomedical case, both processes of energy influx and energy dissipation take some time which is not as simple and quick as the structural load removal in the engineering case. Therefore, the age difference and 3 input behaviors are "dynamic" in nature, i.e. timedependent. *This time-dependent nature leads to a "viscoelastic or viscoplastic" situation.* ***For the author's case, it is "viscoplastic" since most of his biomarkers are continuously improved during the past 13-year time window.***

*Time-dependent output strain and stress of (viscous input*output rate)*

Hooke's law of linear elasticity is expressed as:

Strain (ε: epsilon) = Stress (σ: sigma) / Young's modulus (E)

For biomedical glucose application, his developed linear elastic glucose theory (LEGT) is expressed as:

PPG (strain) = carbs/sugar (stress) * GH.p-Modulus (a positive number) + post-meal walking ksteps * GH.w-Modulus (a negative number)

Where GH.p-Modulus is reciprocal of Young's modulus E.

However, in viscoelasticity or viscoplasticity theory, the stress is expressed as:

Stress = viscosity factor (η: eta) * strain rate (dε/dt)

Where strain is expressed as Greek epsilon or ε.

In this article, in order to construct an "ellipse-like" diagram in a stressstrain space domain (e.g. "hysteresis loop") covering both the positive side and negative side of space, he has modified the definition of strain as follows:

Strain = (body weight at certain specific time instant)

He also calculates his strain rate using the following formula:

Strain rate = (body weight at next time instant) - (body weight at present time instant)

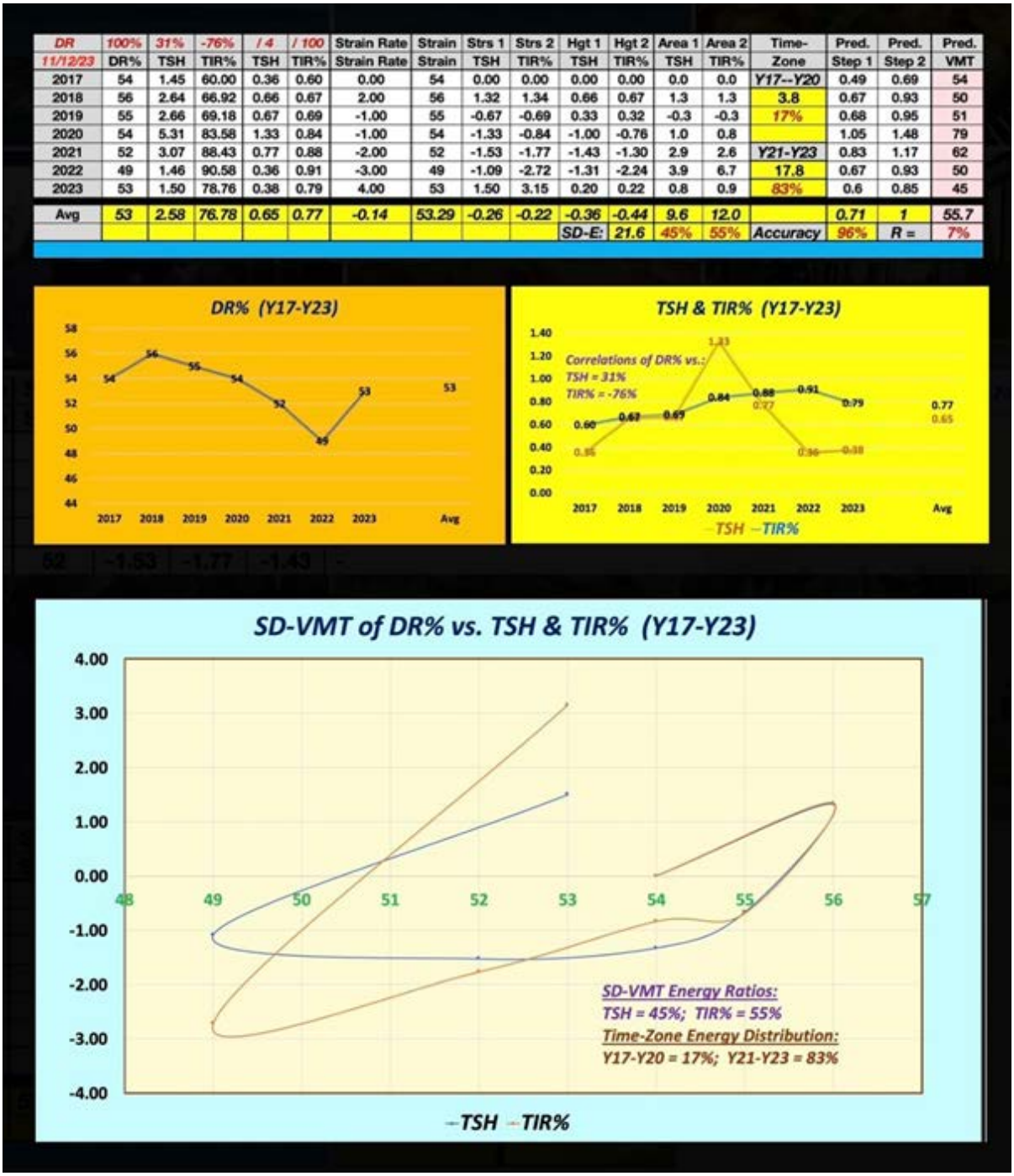
The risk probability % of developing into CVD, CKD, Cancer is calculated based on his developed metabolism index model (MI)

in 2014. His MI value is calculated using inputs of 4 chronic conditions, i.e. weight, glucose, blood pressure, and lipids; and 6 lifestyle details, i.e. diet, drinking water, exercise, sleep, stress, and daily routines. These 10 metabolism categories further contain ~500 elements with millions of input data collected and processed since 2010. For individual deadly disease risk probability %, his mathematical model contains certain specific weighting factors for simulating certain risk percentages associated with different deadly diseases, such as metabolic disorderinduced CVD, stroke, kidney failure, cancers, dementia; artery damage in heart and brain, micro-vessel damage in kidney, and immunity-related infectious diseases, such as COVID death.

Some of explored deadly diseases and longevity characteristics using the ***viscoplastic medicine theory (VMT)*** include stress relaxation, creep, hysteresis loop, and material stiffness, damping effect ***based on time-dependent stress and strain*** which are different from his previous research findings using ***linear elastic glucose theory (LEGT) and nonlinear plastic glucose theory (NPGT).***

2. Results

Figure 1 shows data table, TD analysis results and SD-VMT analysis results.



DR	100%	31%	-76%	/ 4	/ 100	Strain Rate	Strain	Strs 1	Strs 2	Hgt 1	Hgt 2	Area 1	Area 2	Time-	Pred.	Pred.	Pred.
11/12/23	DR%	TSH	TIR%	TSH	TIR%	Strain Rate	Strain	TSH	TIR%	TSH	TIR%	TSH	TIR%	Zone	Step 1	Step 2	VMT
2017	54	1.45	60.00	0.36	0.60	0.00	54	0.00	0.00	0.00	0.00	0.0	0.0	Y17--Y20	0.49	0.69	54
2018	56	2.64	66.92	0.66	0.67	2.00	56	1.32	1.34	0.66	0.67	1.3	1.3	3.8	0.67	0.93	50
2019	55	2.66	69.18	0.67	0.69	-1.00	55	-0.67	-0.69	0.33	0.32	-0.3	-0.3	17%	0.68	0.95	51
2020	54	5.31	83.58	1.33	0.84	-1.00	54	-1.33	-0.84	-1.00	-0.76	1.0	0.8		1.05	1.48	79
2021	52	3.07	88.43	0.77	0.88	-2.00	52	-1.53	-1.77	-1.43	-1.30	2.9	2.6	Y21-Y23	0.83	1.17	62
2022	49	1.46	90.58	0.36	0.91	-3.00	49	-1.09	-2.72	-1.31	-2.24	3.9	6.7	17.8	0.67	0.93	50
2023	53	1.50	78.76	0.38	0.79	4.00	53	1.50	3.15	0.20	0.22	0.8	0.9	83%	0.6	0.85	45
Avg	53	2.58	76.78	0.65	0.77	-0.14	53.29	-0.26	-0.22	-0.36	-0.44	9.6	12.0		0.71	1	55.7
										SD-E:	21.6	45%	55%	Accuracy	96%	R =	7%

Figure 1: Data table, TD analysis results and SD-VMT analysis results

3. Conclusions

In summary, employing traditional statistical correlation, the author noted a low correlation (31%) between his risks of diabetic retinopathy (DR) and his thyroid TSH values. However, a high negative correlation of -76% was found between his DR risk and his TIR % of glucoses, indicating that higher TIR associates with lower DR risk, aligning with the author's expectations.

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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.

For reading more of the author's published VGT or FD analysis results on medical applications, please locate them through platforms for scientific research publications, such as ResearchGate, Google Scholar, etc.