

The GH-Method

Viscoelastic or Viscoplastic Glucose Theory (VGT #65): Estimated Risk Probability Percentages of Having Kidney Cancer and its Moving Trend Over a 7+ Year Period from 1/1/2015 to 4/20/2022 Using a Combined Score of Hyperglycemia, Insulin Resistance, Hypertension, and Albumin-to-Creatinine Ratio, Obesity, Diet, and Exercise as the 4 Key Influential Factors for Developing Kidney Cancer Based on GH-Method: Math-Physical Medicine (No. 654)

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Keywords: Viscoelastic; Viscoplastic; Kidney cancer; Type 2 diabetes; Hyperglycemia; Insulin resistance; Hypertension; Albumin-to-creatinine ratio; Obesity; Diet; Exercise; Fasting plasma glucose; Postprandial plasma glucose

Abbreviations: T2D: type 2 diabetes; SD: space domain; TD: time domain; MI: metabolism index; PPG: postprandial plasma glucose; FPG: fasting plasma glucose; MPM: math-physical medicine

1. INTRODUCTION

Recently, the author read a few published medical articles regarding kidney cancer. He then outlines some key information in the Introduction section. The selected information sources have been referenced within this section and will not be listed in the Reference section.

“Kidney Care:

The first paper from the UK covers the general care of kidneys which provides useful information.

(1) www.kidneycareuk.org

Diabetes mellitus (DM) is a common condition, affecting around 7% of the UK population. It is the most common cause of chronic kidney disease (CKD), responsible for around a third of people needing kidney replacement therapy (dialysis or preemptive kidney transplant).

Diabetes is a serious condition where the glucose (sugar) levels in your blood are too high. You get glucose from food and drink and it is moved from the blood to your cells by a hormone called insulin which is made in the pancreas. There are two main types of diabetes:

- Type 1 usually starts in childhood or adolescence, although it can occur at any age. People with type 1 diabetes can't make any insulin themselves as their bodies attack the cells in the pancreas that normally make it;
- Type 2 usually starts in middle age although it is becoming increasingly common in younger people. People with type 2 diabetes produce some insulin but it is not effective and over time not enough is made.

In both types of diabetes, because the glucose can't get into your cells, it builds up in the blood. If left untreated, high glucose levels can cause serious damage to your body,

including your eyes, heart, feet, and kidneys. Whichever type of DM you have, even when diabetes is controlled, the disease can lead to kidney problems. Fortunately, most people with diabetes do not develop a kidney problem that is severe enough to progress to end-stage renal disease (ESRD), requiring dialysis and/or a transplant.

Diabetes-related kidney disease accounts for 27.5% of new cases of kidney failure. Diabetes can affect your kidneys in two main ways:

1. Kidney disease (diabetic nephropathy). High glucose levels cause extra blood to flow through the tiny filters in your kidneys, so they have to work harder than normal to clean them. Over time this can damage the filters, causing them to leak.
2. Disease of the kidney's blood vessels (renovascular disease). High blood pressure causes a 'furring up' of the artery to the kidney, reducing the blood supply and causing scarring.

Kidney damage occurs slowly over many years. It can be identified in its early stages by very small amounts of protein in the urine. This protein has leaked from the kidneys as a result of the damage to the filters. It is therefore important that people with diabetes are screened regularly for kidney disease to find and treat any problems early before more serious damage can occur.

What other problems can diabetes and kidney disease cause?

Both diabetes and kidney disease can cause high blood pressure which increases the risk of heart attacks and strokes. Foot and eye problems are also common in people with diabetes and kidney disease, but these can be preventable. Regular checks with your GP and optician are therefore important to try to stop any problems from developing or to spot them early on when they can be easier to treat.

How will my kidneys be monitored if I have diabetes?

Your diabetes will be monitored by your GP. It is very important to have your urine tested at least once a year, as protein leaking into the urine is the first sign of kidney damage. It is important to pick this up early as there

are many treatments to protect your kidneys from further damage.

You will also have regular blood tests to check your kidney function. If your kidney damage progresses, you will be referred to a kidney specialist (nephrologist) at the hospital to discuss treatment options. All people with diabetes should keep their BP below 130/80.

How is diabetes treated?

Diabetes is a life-long condition that needs regular monitoring. Type 1 diabetes is treated by multiple daily insulin injections or an insulin pump. When you are first diagnosed you will be shown how to do these injections yourself at home. You will need to continue to do these injections yourself to maintain your health. This can seem very overwhelming at first but you will receive support from your healthcare team.

Type 2 diabetes is usually treated with key lifestyle changes, including changing your diet, increasing the amount of exercise you do, and trying to lose weight. Most people with type 2 diabetes will also be offered medication. This is usually in the form of tablets to start with, although insulin injections may also be needed eventually.

A course on kidney disease:

Diabetic kidney disease takes many years to develop. People who are developing kidney disease will have small amounts of a blood protein called albumin leaking into their urine. This first stage is called microalbuminuria. Kidney function usually remains normal during this period. As the disease progresses, more albumin leaks into the urine. This stage is called proteinuria.

As kidney damage develops, blood pressure often rises. Later on, chronic kidney disease (CKD) develops. At this stage, you may experience ankle swelling and shortness of breath (due to water in the lungs). It usually takes at least 10 years to get to this point. Dialysis may be necessary.

How do you know you have kidney disease?

People with DM should be screened regularly for kidney disease. The key markers for kidney disease are serum creatinine (and a

formula called (eGFR) and the urine protein level.

Effects of high blood pressure:

Both a family history of DM with complications and the presence of hypertension (high blood pressure, BP), increase the chances of developing kidney disease in people with diabetes. Hypertension also accelerates the progress of kidney disease when it already exists.

Treatment of even mild hypertension is essential for people with DM.

How can I look after my kidneys if I have diabetes?

- Stop smoking. Smoking is a health risk for everyone, but for people with diabetes, the risk is even greater. It can make your kidney disease worse and contribute to heart attacks and strokes.

- Keep your blood pressure under control. You should aim for a blood pressure of 130/80 or less. Your kidney team may prescribe medication to help with this. You can buy a blood pressure machine at your local chemist to check your blood pressure at home to help keep it under control.

- Keep your cholesterol level within the range recommended by your doctor or nurse. This may involve a change in diet and/or medication. Ask your kidney team to refer you to a dietician.

- Lose weight if you are overweight. Talk to your GP about safe ways to lose weight if this applies to you.

- Keep active and eat a healthy balanced diet. It is recommended that everyone takes part in at least 30 minutes of moderate physical activity daily.

- Keep your alcohol intake to 14 units a week or less.

You must take responsibility for your health. Go to all your appointments, learn the best ways to control your blood pressure and blood glucose levels, and get support to take as much control of your health as possible. Your healthcare team can help you to manage your diabetes and improve your overall health.

Preventing and slowing kidney disease

- Stopping smoking. Smoking is a health risk for everyone, but for people with diabetes, the risk is even greater. Along with DM, it causes renovascular and worsens kidney disease, as well as contributing to heart attacks and strokes. Try to give up - your GP can help.

- BP tablets. Drugs used to lower BP (to 130/80, or lower) can slow the progression of kidney disease significantly. Two types of drugs, angiotensin receptor blockers (ARB), are effective in slowing the progression of kidney disease. Patients with even mild BP or persistent microalbuminuria (first stage of diabetic kidney disease), should have low BP preferably taking an ACEi or ARB.

- Other treatments. Keeping blood sugar well controlled may help, especially for those in the early stages of kidney disease. Lowering cholesterol to <5.0 mmol/L with a drug called a 'statin' may also be of benefit.

Dialysis and transplantation:

When people with diabetes experience ESRD they need either dialysis or a kidney transplant. Some patients with Type 1 DM can have a 'double' (kidney-pancreas) transplant. Currently, the survival of kidneys transplanted into people with DM is about the same as the survival of transplants in people without DM (about 10-15 years). Dialysis for people with diabetes also works well in the short run.

Find out more:

You can also find out more about diabetes on the following websites: -

- Diabetes UK
- NHS diabetes page”

Kidney cancer:

The following papers No. 2 through No. 8 focus on kidney cancers.

(2) US News and Reports

Kidney Cancer and Type 2 Diabetes: What's the Connection?

Research highlights an increase in renal cancer risk among diabetics, especially women by S. Adam Ramin, MD.

Aug. 2, 2018, at 6:00 a.m

Kidney Cancer and Type 2 Diabetes: Cancer affecting the kidneys and renal pelvis rank among the top 10 most common cancers in the world, with renal cell carcinoma the most frequently diagnosed kidney cancer type. And though this type of cancer affects a variety of people around the globe, it's particularly on the rise in the more developed regions, including North America and Europe. For the last several years, a majority of evidence has pointed to smoking, hypertension, and obesity as the most established risk factors. But new research further highlights the significant influence that diabetes plays in the development of RCC, especially among the female population. To start, a brief explanation of diabetes is in order. The medical term for this group of diseases that affect how the human body uses glucose is diabetes mellitus, and it's classified into two types. Type 1 diabetes can develop at any age, though it most frequently first appears during childhood or the teen years. Type 2 diabetes is the most common diabetes type, and while it can develop at any age, it most often presents in people over age 40. A just-right balance of glucose in the blood stream is essential because it provides the cell energy that comprises our muscles and tissues. And it's also the brain's main fuel source. Diabetes elevates glucose levels beyond the normal balance and can result in a number of symptoms and health risks, including kidney damage and increased kidney cancer risk.

5 Ways to Reduce Your Risk of Developing Kidney Disease:

Though the purpose of this study was not necessarily intended to identify a cause for the diabetes-kidney cancer connection, there's plenty we do know about the risk factors for each that can help everyone (not just women) reduce their risk. Your doctor is a great first place to start. He or she can help you manage a diabetic condition while you take the initiative to make healthy lifestyle changes on your own that can reverse the effects all together in some cases. This has a significant amount to do with your diet. It needs to be rich in a variety of fruits and vegetables, while also reducing and

eliminating highly processed foods or those loaded with added sugar. While this may seem easier said than done, there are at least a few meal subscription services that have made a commitment to offering customers meal plans tailored to their dietary needs, including those trying to manage diabetes. Increasing physical activity is another important way to help manage and stave off diabetic conditions. Aim for 30 minutes of heart-pumping activity each day, and go slow at first if you need to. Finally, if you smoke, take the steps to quit now. You'll be doing so much more for your overall health than just reducing your kidney cancer risk. It's worth it.

(3) www.ncbi.nlm.nih.gov

Type 2 Diabetes Mellitus and Kidney Cancer Risk: A Retrospective Cohort Analysis of the National Health Insurance by Chin-Hsiao Tseng.

The 3-year cumulative incidence of kidney cancer in diabetic patients and non-diabetic people was 166.9 and 33.1 per 100,000 person-years, respectively. The incidence increased with regard to increasing age in both the diabetic patients and the non-diabetic people, but a higher risk of kidney cancer for the diabetic patients compared to the non-diabetic people was consistently observed in different age groups. After multivariable adjustment, the odds ratio for diabetic patients versus non-diabetic people was 1.7 (95% confidence interval: 1.3–2.1, $P < 0.01$). While compared to the non-diabetic people, the odds ratio (95% confidence interval) for diabetes duration < 1 , 1–2.9 years, 3–4.9 years and ≥ 5 years was 1.5 (0.8–2.7), 1.6 (1.0–2.4), 1.6 (1.1–2.4) and 1.7 (1.3–2.3), respectively (P -trend < 0.01). Analyses conducted on the diabetic patients and the non-diabetic people, respectively, consistently showed age, nephropathy, and end-stage renal disease as significant risk factors for kidney cancer. Additionally, living in the metropolitan Taipei region might also be associated with a higher risk of kidney cancer in the non-diabetic people, indicating a potential link.

Conclusions

Patients with type 2 diabetes mellitus have a significantly higher risk of kidney cancer.

(4) Mechanisms through which diabetes mellitus influences renal cell carcinoma development and treatment: A review of the literature.

Authors: Dominika Labochka Barbara Moszczuk Wojciech Kukwa Cezary Szczylik Anna M. Czarneck, Published online on: October 17, 2016
<https://doi.org/10.3892/ijmm.2016.2776>
Pages: 1887-1894

Abstract

Renal cell carcinoma (RCC) comprises 2-3% of all malignant tumors in adults. Many studies have established the key roles of smoking, hypertension, and other components of metabolic syndrome in the occurrence of RCC. Diabetes mellitus (DM), one of the main consequences of metabolic syndrome, appears much more often in patients with RCC. The prognosis for patients suffering from both diabetes and RCC is worse than for those with kidney cancer only. Diabetes is linked to a higher rate of recurrence and a greater number of distant metastases. These factors contribute to a reduction in overall survival (OS) and cause-specific survival (CSS). Studies and case reports have shown that they influence blood glucose levels (BGLs) in diabetic patients, sometimes causing dangerous episodes of hypoglycemia. Hyperinsulinemia and hyperglycemia can be considered independent carcinogenic factors, as they increase the amount of pro-inflammatory cytokines, reactive oxygen species, and lipid peroxidation.

(5) www.curetoday.com

Women With Diabetes May Face Increased Kidney Cancer Risk by Antonia DePace, July 26, 2021.

Post-menopausal women may be at an increased risk for kidney cancer if they are diagnosed with type 2 diabetes. Post-menopausal women without obesity who were previously diagnosed with type 2 diabetes may be at an increased risk for developing kidney cancer. Findings from the study published in *Maturitas* highlight the potential need for more surveillance for cancer in this specific patient population. "The number of kidney cancer cases has been increasing for several decades, so we think it

is important to identify risk factors of kidney cancer to aid in early detection," explained lead study author Shuo Wang, a Ph.D. student from the division of epidemiology and community health at the University of Minnesota School of Public Health, in an interview with CURE®.

The Centers for Disease Control and Prevention estimates that there are 64,000 new cases of kidney cancer annually. Likewise, diabetes affects more than 34 million Americans today, of which 90% to 95% have type 2 diabetes (when the body builds a resistance to insulin, a hormone made by the pancreas that allows blood sugar cells to be used as energy).

During 25 years of follow-up, 245 post-menopausal women received a diagnosis of kidney cancer among the 36,975 women included in this study.

When researchers took age into consideration, there was a significant link between diabetes and the risk for kidney cancer. The relationship between diabetes and kidney cancer weakened when several other factors were assessed like body mass index, hypertension (high blood pressure), waist-to-hip ratio (an estimate of how much fat is stored on the hips, waist and buttocks), diuretic use, physical activity, alcohol intake, number of cigarette packs smoked per year and total caloric intake.

Researchers also assessed the risk for kidney cancer in women without obesity (body mass index less than 30 kg/m²) and those with a waist circumference less than 34.6 inches. Type 2 diabetes in these women was significantly associated with the risk for kidney cancer.

Wang noted that the relation between type 2 diabetes and kidney cancer is likely due to several mechanisms: higher levels of insulin-like growth factor 1, which can trigger tumor growth, and higher blood glucose levels, which may increase the risk of cancer. Additionally, not finding an association between type 2 diabetes and kidney cancer in patients with obesity may be because obese patients even without type 2 diabetes may have abnormal metabolic profiles that may increase their risk of cancer. According to Wang, adding more surveillance for patients diagnosed with type 2 diabetes may lead to

potential early detection and better survival outcomes. “Patients with type 2 diabetes may need more surveillance for cancer, including kidney cancer,” she said.

Wang noted limitations of the study was the inclusion of primarily White post-menopausal women. She said, “The study may not be generalizable to male or non-White patients.”

For next steps, Wang says that there needs to be more focus on diabetes and its association to risk of kidney cancer in order to fully validate their results.

(6) Increased kidney cancer risk in diabetes mellitus patients: a population-based cohort study in Lithuania.

Greta Undzyte, Ausvydas Patasius, Donata Linkeviciute-Ulinskiene, Lina Zabuliene, Rimantas Stukas, Audrius Dulskas
Pages 1241-1245 | Received 16 Mar 2020, Accepted 08 Apr 2020, Published online: 28 Apr 2020.

Abstract

Background

Diabetes is associated with increased risk of various cancers but its association with kidney cancer is unclear. The objective of this study was to evaluate the association between T2DM with or without metformin use and the risk of kidney cancer in a population-based national cohort in Lithuania.

Methods

The cohort was composed of diabetic patients identified in the NHIF database during 2000–2012. Cancer cases were identified by record linkage with the national Cancer Registry. Standardized incidence ratios (SIRs) for kidney cancer as a ratio of observed number of cancer cases in diabetic patients to the expected number of cancer cases in the underlying general population were calculated.

Results

T2DM patients (11,592) between 2000 and 2012 were identified. Overall, 598 cases of primary kidney cancer were identified versus 393.95 expected yielding an overall SIR of 1.52 (95% CI: 1.40–1.64). Significantly higher risk was found in males and females.

Significantly higher risk of kidney cancer was also found in both metformin users and never-users’ groups (SIRs 1.45, 95% CI: 1.33–1.60 and 1.78 95% CI: 1.50–2.12, respectively).

Conclusions

The patients with T2DM have higher risk for kidney cancer compared with the general Lithuanian population.

(7) Diabetes and kidney cancer survival in patients undergoing nephrectomy: A Canadian multi-center, propensity score analysis, [Pubmed.ncbi.nlm.nih.gov](https://pubmed.ncbi.nlm.nih.gov)

Madhur Nayan 1 , Shreya Jalali 2 , Anil Kapoor 3 , Antonio Finelli 1 , Alan So 4 , Ricardo Rendon 5 , Rodney H Breau 6 , Luke T Lavalley 6 , Simon Tanguay 7 , Daniel Heng 8 , Jun Kawakami 9 , Naveen S Basappa 10 , Georg Bjarnason 11 , Frederic Pouliot 12 , Robert J Hamilton 13
PMID: 31285115 DOI: 10.1016/j.urolonc.2019.06.006.

Abstract

Introduction:

Diabetes has been associated with worse survival outcomes in various malignancies; however, there are conflicting data in kidney cancer. Determining whether diabetes is associated with survival in kidney cancer may help guide treatment in a comorbid patient population.

Methods:

We used the Canadian Kidney Cancer information system database to identify patients undergoing partial or radical nephrectomy between 1989 and 2017 for localized renal cell carcinoma at 16 institutions across Canada. We derived inverse probability of treatment weights (IPTW) from a propensity score model based on various clinical, surgical, and pathological characteristics. We used Cox proportional hazard models to evaluate the association between diabetes and cancer-specific and overall survival, in the sample weighted by the IPTW.

Results:

4828 patients met inclusion criteria, of whom 948 (19.6%) were diabetic. Median follow-up in those without death was 26.6 months (interquartile range 9.7-53.8). Among the

entire cohort, 901 deaths were from any cause, and 299 deaths from kidney cancer. Before propensity score methods, diabetics were older, more likely to have comorbidities and clear cell histopathology. After propensity score adjustment, all characteristics were balanced between groups (standardized difference <0.10). IPTW-adjusted Cox proportional hazard models demonstrated no significant association between diabetes and cancer-specific (hazard ratio 1.13, 95% confidence interval 0.78-1.62), or overall survival (hazard ratio 1.14, 95% confidence interval 0.94-1.38).

Conclusions:

Our multi-centre study found that diabetes and nondiabetics have similar survival following nephrectomy for kidney cancer.

(8) History of treated hypertension and diabetes mellitus and risk of renal cell cancer by A. Zucchetto, L. Dal Maso, A. Tavani, E. Negri, S. Franceschi, C. La Vecchia, *Annals of Oncology*,
OpenArchiveDOI:<https://doi.org/10.1093/annonc/mdl438>.

ABSTRACT

Background:

An increased risk of renal cell cancer (RCC) has been reported in subjects with hypertension. Whether this association may vary according to sex, smoking, obesity, or RCC clinical presentation is unclear. Results on the link between diabetes mellitus and RCC are inconclusive.

Patients and methods:

We conducted an Italian multicenter case-control study, including 767 (494 men, 273 women) incident cases of RCC, under 80 years of age, and 1534 hospital controls, frequency-matched to cases. Multiple logistic regression models, conditioned to center, sex, and age, and adjusted for period of interview, education, smoking, and body mass were used to estimate odds ratios (OR).

Results:

Compared with subjects never treated, patients with a history of treated hypertension [OR = 1.7, 95% confidence interval (CI) 1.4-2.1] reported an excess risk of RCC. This pattern was confirmed in different strata of sex, education, smoking

habits, body mass, tumor histological type, stage, or grade. The attributable risk of RCC for treated hypertension in this population was 16%. A slight, nonsignificant increased risk was found for history of diabetes mellitus (OR = 1.3, 95% CI 0.9-1.7).

Conclusion:

A possible causal role of hypertension in renal cell carcinogenesis is supported by the consistency of the direct association.”

From these above-quoted 8 papers, diabetes has been identified either directly related to or inconclusive about its relationship with kidney cancers; however, both obesity and chronic kidney disease (CKD) have been mentioned as known risk factors. As we know, diet and exercise are directly related to obesity and T2D; therefore, the author can safely draw a picture which includes several “modifiable influential factors of kidney cancers” with their respective weighting factors as depicted below:

Diabetes, blood pressure & CKD, including hyperglycemia (PPG > 180 mg/dL), insulin resistance (FPG > 180 mg/dL), hypertension score, and albumin-to-creatinine ratio (ACR): 40%

Obesity or being overweight: 30%

Diet including both quantity and quality of food and meals: 15%

Daily walking exercise: 15%

As a result, relative kidney cancer risk can then be defined as follows:

Relative kidney cancer risk %

= (hyperglycemia + insulin resistance + hypertension + ACR) * 40% + obesity * 30% + diet * 15% + exercise * 15%

The author’s stringent lifestyle management efforts during the past 12+ years, including both diet and exercise, are directly beneficial to his weight reduction, glucose control, and metabolism improvements. It is necessary to provide a brief description of his health history.

He was diagnosed with T2D in 1997 with a random glucose check at a 300 mg/dL level; however, his T2D condition most likely began earlier. He suffered his first two chest pain episodes in 1993-1994 and three more heart episodes until 2007. His primary physician

informed him that he had diabetic kidney issues in 2010. He then consulted with two more clinical doctors who advised him to immediately start insulin injections and kidney dialysis. This was his wake-up call. He then decided to save his life by conducting his study and research on food nutrition and chronic diseases that same year. His health profile in 2010 was: body weight at 220 lbs. (BMI 32), average glucose at 280 mg/dL, fasting plasma glucose (FPG) in the early morning at 180 mg/dL, lab-tested HbA1C at 10%, triglycerides at 1160 mg/dL (target: <150 mg/dL), and his ACR at 116 (target: <30). In addition, by 2010, he has also suffered a total of 5 heart episodes, foot ulcer, hypothyroidism, diabetic retinopathy, etc.

Over the past 13 years, he has made significant lifestyle changes. For example, he consumes less than 20 grams of carbohydrates and sugar per meal, stops eating processed food, reduces his food quantity by 50%, walks 6-7 miles or 10-11 kilometers daily, sleeps 7-8 hours each night, and avoids stress as much as possible. As a matter of fact, he has never drunk alcohol, smoked cigarettes, or used any illicit drugs in his life.

As of April 10, 2022, his health profile for the first 3 months of 2022 was: body weight at 169 lbs. (BMI 24.95), daily average glucose at 106 mg/dL, FPG in the early morning at 94 mg/dL, lab-tested A1C at 5.8%, triglycerides at 108, and ACR at 16. A significant accomplishment since he discontinued taking 3 different kinds of diabetes medications on 12/8/2015. Fortunately, he has not detected any sign of cancer to date.

2. METHODS

To offer a simple explanation to readers who do not have a physics or engineering background, the author includes a brief excerpt from Wikipedia regarding the description of basic concepts for elasticity and plasticity theories, viscoelasticity, and viscoplasticity theories from the disciplines of engineering and physics, and his developed metabolism index (MI) Model in this method section.

2.1 Relationships between biomedical causes and biomedical symptoms

As a mathematician/engineer over 40 years and now conducting his medical research work for the past 13 years, the author has discovered that people frequently seek answers, illustrations, or explanations for the relationships between the input variable (force applied on a structure or cause of a disease) and output variable (deformation of a structure or symptom of a disease). However, the multiple relationships between input and output could be expressed with many different matrix formats of 1×1 , $1 \times n$, $m \times 1$, or $m \times n$ (m or n means different multiple variables). In addition to these described mathematical complications, the output resulting from one or more inputs can also become an input of another output, which is a symptom of certain causes that can become a cause of another different symptom. This phenomenon is indeed a complex scenario with “chain effects”. In fact, both engineering and biomedical complications are fundamentally mathematical problems that correlate or conform with many inherent physical laws or principles. In his medical research work, he has encountered more than 100 different sets of biomarkers with almost equal or more amounts of causes (or input variables) and symptoms (or output variables).

Since December of 2021, the author applied theories of viscoelasticity and viscoplasticity (VGT) from physics and engineering disciplines to investigate more than 60 sets of input/output biomarkers, including nearly 10 sets of cancer cases. The purpose is to identify certain hidden relationships between certain output biomarkers, such as cancer risk, and its corresponding multiple inputs, such as glucose, blood pressure, blood lipids, obesity or overweight, and metabolism index of 6 lifestyle details and 4 chronic diseases. In this study, the hidden biophysical behaviors and possible inter-relationships among the output symptom and multiple input causes are “time-dependent” and change from time to time. These important time-dependency characteristics provide insight into the cancer risk’s moving pattern. It also controls the cancer risk curve shape, the associated energy created, stored, or burned inside during the process of stress up-loading (moving upward or increasing) and stress down-loading (moving downward or decreasing) of the input biomarkers with the output biomarker of cancer risk %. This VGT application emphasizes the time-dependency

characteristics of involved variables. In the medical field, most biomarkers are time-dependent since body organ cells are organic in nature and change all of the time. Incidentally, VGT can generate a stress-strain curve or cause-symptom curve, known as a “hysteresis loop” in physics, in which area size can also be used to estimate the relative energy created, stored, or burned during the process of uploading (e.g., increasing glucose) and unloading (e.g., decreasing body weight) over the timespan of the cancer risk %. He calls this relative energy the “VGT energy”.

It should be emphasized here that both cancer risk % and its associated VGT energy are estimated relative values, not “absolute” values.

The following defined stress and strain equations are used to establish the VGT stress-strain diagram in a space domain (SD):

VGT strain
 = ϵ (symptom)
 = individual symptom at the present time

VGT stress
 = σ (based on the change rate of strain, symptom, multiplying with one or more viscosity factors or influential factors)
 = $\eta * (d\epsilon/dt)$
 = $\eta * (d\text{-strain}/d\text{-time})$
 = (viscosity factor η using normalized factor at present time) * (symptom at present time - symptom at a previous time)

Where the strain is the cancer risk percentage and the stress is his cancer risk change rate multiplied by several chosen input biomarkers as the individual viscosity factor. In his VGT studies, sometimes, he carefully selects certain normalization factors for each input biomarker, respectively. The normalization factors are the dividing lines between a healthy state and an unhealthy state. For example, 170 lbs. for body weight, 6.0 for HbA1C, 120 mg/dL for glucose, 180 mg/dL for hyperglycemia, 73.5% for overall MI score, and 10,000 steps for daily walking exercise, etc.

2.2 Elasticity, plasticity, viscoelasticity, and viscoplasticity

The difference between elastic materials and viscoelastic materials (from “Soborthans, innovating shock and vibration solutions”).

What are elastic materials?

Elasticity is the tendency of solid materials to return to their original shape after forces are applied on them. When the forces are removed, the object will return to its initial shape and size if the material is elastic.

What are viscous materials?

Viscosity is a measure of a fluid’s resistance to flow. A fluid with large viscosity resists motion. A fluid with low viscosity flows. For example, water flows more easily than syrup because it has a lower viscosity. High viscosity materials might include honey, syrups, or gels – generally things that resist flow. Water is a low viscosity material, as it flows readily. Viscous materials are thick or sticky or adhesive. Since heating reduces viscosity, these materials don’t flow easily. For example, warm syrup flows more easily than cold.

What is viscoelastic?

Viscoelasticity is the property of materials that exhibit both viscous and elastic characteristics when undergoing deformation. Synthetic polymers, wood, and human tissue, as well as metals at high temperature, display significant viscoelastic effects. In some applications, even a small viscoelastic response can be significant.

Elastic behavior versus viscoelastic behavior

The difference between elastic materials and viscoelastic materials is that viscoelastic materials have a viscosity factor and the elastic ones don’t. Because viscoelastic materials have the viscosity factor, they have a strain rate dependent on time. Purely elastic materials do not dissipate energy (heat) when a load is applied, then removed; however, a viscoelastic substance does.

The following brief introductions are excerpts from Wikipedia:

“Elasticity (physics):

The physical property when materials or objects return to original shape after deformation.

In physics and materials science, elasticity is the ability of a body to resist a distorting influence and to return to its original size and shape when that influence or force is removed. Solid objects will deform when adequate loads are applied to them; if the material is elastic, the object will return to its initial shape and size after removal. This is in contrast to plasticity, in which the object fails to do so and instead remains in its deformed state.

The physical reasons for elastic behavior can be quite different for different materials. In metals, the atomic lattice changes size and shape when forces are applied (energy is added to the system). When forces are removed, the lattice goes back to the original lower energy state. For rubbers and other polymers, elasticity is caused by the stretching of polymer chains when forces are applied.

Hooke's law states that the force required to deform elastic objects should be directly proportional to the distance of deformation, regardless of how large that distance becomes. This is known as perfect elasticity, in which a given object will return to its original shape no matter how strongly it is deformed. This is an ideal concept only; most materials which possess elasticity in practice remain purely elastic only up to very small deformations, after which plastic (permanent) deformation occurs.

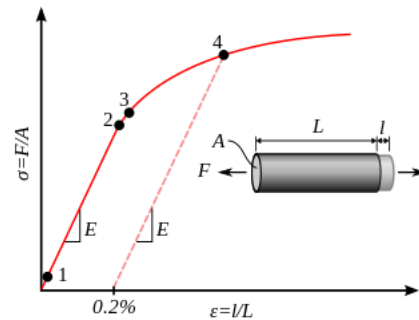
In engineering, the elasticity of a material is quantified by the elastic modulus such as the Young's modulus, bulk modulus or shear modulus which measure the amount of stress needed to achieve a unit of strain; a higher modulus indicates that the material is harder to deform. The material's elastic limit or yield strength is the maximum stress that can arise before the onset of plastic deformation.

Plasticity (physics):

Deformation of a solid material undergoing non-reversible changes of shape in response to applied forces.

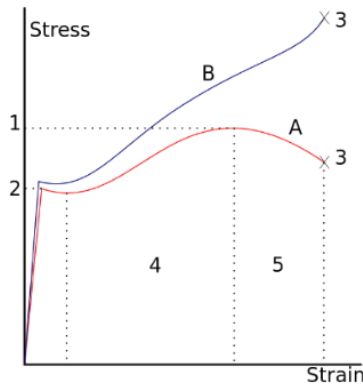
In physics and materials science, plasticity, also known as plastic deformation, is the

ability of a solid material to undergo permanent deformation, a non-reversible change of shape in response to applied forces. For example, a solid piece of metal being bent or pounded into a new shape displays plasticity as permanent changes occur within the material itself. In engineering, the transition from elastic behavior to plastic behavior is known as yielding.



Stress–strain curve showing typical yield behavior for nonferrous alloys.

1. True elastic limit
2. Proportionality limit
3. Elastic limit
4. Offset yield strength



A stress–strain curve typical of structural steel.

- 1: Ultimate strength
- 2: Yield strength (yield point)
- 3: Rupture
- 4: Strain hardening region
- 5: Necking region
- A: Apparent stress (F/A_0)
- B: Actual stress (F/A)

Plastic deformation is observed in most materials, particularly metals, soils, rocks, concrete, and foams. However, the physical mechanisms that cause plastic deformation

can vary widely. At a crystalline scale, plasticity in metals is usually a consequence of dislocations. Such defects are relatively rare in most crystalline materials, but are numerous in some and part of their crystal structure; in such cases, plastic crystallinity can result. In brittle materials such as rock, concrete and bone, plasticity is caused predominantly by slip at microcracks. In cellular materials such as liquid foams or biological tissues, plasticity is mainly a consequence of bubble or cell rearrangements, notably T1 processes.

For many ductile metals, tensile loading applied to a sample will cause it to behave in an elastic manner. Each increment of load is accompanied by a proportional increment in extension. When the load is removed, the piece returns to its original size. However, once the load exceeds a threshold – the yield strength – the extension increases more rapidly than in the elastic region; now when the load is removed, some degree of extension will remain.

Elastic deformation, however, is an approximation and its quality depends on the time frame considered and loading speed. If, as indicated in the graph opposite, the deformation includes elastic deformation, it is also often referred to as "elasto-plastic deformation" or "elastic-plastic deformation".

Perfect plasticity is a property of materials to undergo irreversible deformation without any increase in stresses or loads. Plastic materials that have been hardened by prior deformation, such as cold forming, may need increasingly higher stresses to deform further. Generally, plastic deformation is also dependent on the deformation speed, i.e. higher stresses usually have to be applied to increase the rate of deformation. Such materials are said to deform viscoplastically.”

Viscoelasticity:

Property of materials with both viscous and elastic characteristics under deformation. In materials science and continuum mechanics, viscoelasticity is the property of materials that exhibit both viscous and elastic characteristics when undergoing deformation. Viscous materials, like water, resist shear flow and strain linearly with time when a stress is applied. Elastic

materials strain when stretched and immediately return to their original state once the stress is removed.

Viscoelastic materials have elements of both of these properties and, as such, exhibit time-dependent strain. Whereas elasticity is usually the result of bond stretching along crystallographic planes in an ordered solid, viscosity is the result of the diffusion of atoms or molecules inside an amorphous material.

In the nineteenth century, physicists such as Maxwell, Boltzmann, and Kelvin researched and experimented with creep and recovery of glasses, metals, and rubbers. Viscoelasticity was further examined in the late twentieth century when synthetic polymers were engineered and used in a variety of applications. Viscoelasticity calculations depend heavily on the viscosity variable, η . The inverse of η is also known as fluidity, ϕ . The value of either can be derived as a function of temperature or as a given value (i.e., for a dashpot).

Depending on the change of strain rate versus stress inside a material, the viscosity can be categorized as having a linear, non-linear, or plastic response. When a material exhibits a linear response, it is categorized as a Newtonian material. In this case the stress is linearly proportional to the strain rate. If the material exhibits a non-linear response to the strain rate, it is categorized as non-Newtonian fluid. There is also an interesting case where the viscosity decreases as the shear/strain rate remains constant. A material which exhibits this type of behavior is known as thixotropic. In addition, when the stress is independent of this strain rate, the material exhibits plastic deformation. Many viscoelastic materials exhibit rubber like behavior explained by the thermodynamic theory of polymer elasticity.

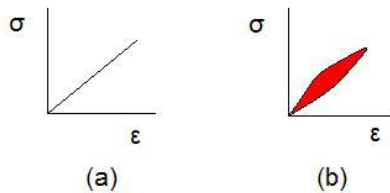
Cracking occurs when the strain is applied quickly and outside of the elastic limit. Ligaments and tendons are viscoelastic, so the extent of the potential damage to them depends both on the rate of the change of their length as well as on the force applied.

A viscoelastic material has the following properties:

- hysteresis is seen in the stress–strain curve

- stress relaxation occurs: step constant strain causes decreasing stress
- creep occurs: step constant stress causes increasing strain
- its stiffness depends on the strain rate or the stress rate.

Elastic versus viscoelastic behavior



Stress–strain curves for a purely elastic material (a) and a viscoelastic material (b). The red area is a hysteresis loop and shows the amount of energy lost (as heat) in a loading and unloading cycle. It is equal to

$$\oint \sigma d\epsilon$$

where σ is stress and ϵ is strain.

Unlike purely elastic substances, a viscoelastic substance has an elastic component and a viscous component. The viscosity of a viscoelastic substance gives the substance a strain rate dependence on time. Purely elastic materials do not dissipate energy (heat) when a load is applied, then removed. However, a viscoelastic substance dissipates energy when a load is applied, then removed. Hysteresis is observed in the stress–strain curve, with the area of the loop being equal to the energy lost during the loading cycle. Since viscosity is the resistance to thermally activated plastic deformation, a viscous material will lose energy through a loading cycle. Plastic deformation results in lost energy, which is uncharacteristic of a purely elastic material's reaction to a loading cycle.

Specifically, viscoelasticity is a molecular rearrangement. When a stress is applied to a viscoelastic material such as a polymer, parts of the long polymer chain change positions. This movement or rearrangement is called “creep”. Polymers remain a solid material even when these parts of their chains are rearranging in order to accompany the stress, and as this occurs, it creates a back stress in the material. When the back stress is the same magnitude as the applied stress, the

material no longer creeps. When the original stress is taken away, the accumulated back stresses will cause the polymer to return to its original form. The material creeps, which gives the prefix visco-, and the material fully recovers, which gives the suffix -elasticity.

Viscoplasticity:

Viscoplasticity is a theory in continuum mechanics that describes the rate-dependent inelastic behavior of solids. Rate-dependence in this context means that the deformation of the material depends on the rate at which loads are applied. The inelastic behavior that is the subject of viscoplasticity is plastic deformation which means that the material undergoes unrecoverable deformations when a load level is reached. Rate-dependent plasticity is important for transient plasticity calculations. The main difference between rate-independent plastic and viscoplastic material models is that the latter exhibit not only permanent deformations after the application of loads but continue to undergo a creep flow as a function of time under the influence of the applied load.

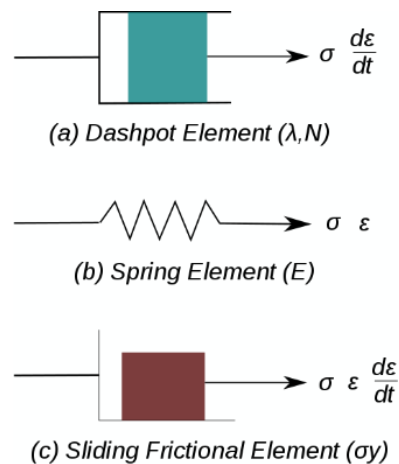


Figure 1. Elements used in one-dimensional models of viscoplastic materials.

The elastic response of viscoplastic materials can be represented in one-dimension by Hookean spring elements. Rate-dependence can be represented by nonlinear dashpot elements in a manner similar to viscoelasticity. Plasticity can be accounted for by adding sliding frictional elements as shown in Figure 1. In the figure E is the modulus of elasticity, λ is the viscosity parameter and N is a power-law type parameter that represents non-linear

dashpot [$\sigma(d\epsilon/dt) = \sigma = \lambda(d\epsilon/dt)(1/N)$]. The sliding element can have a yield stress (σ_y) that is strain rate dependent, or even constant, as shown in Figure 1c.

Viscoplasticity is usually modeled in three-dimensions using overstress models of the Perzyna or Duvaut-Lions types. In these models, the stress is allowed to increase beyond the rate-independent yield surface upon application of a load and then allowed to relax back to the yield surface over time. The yield surface is usually assumed not to be rate-dependent in such models. An alternative approach is to add a strain rate dependence to the yield stress and use the techniques of rate independent plasticity to calculate the response of a material.

For metals and alloys, viscoplasticity is the macroscopic behavior caused by a mechanism linked to the movement of dislocations in grains, with superposed effects of inter-crystalline gliding. The mechanism usually becomes dominant at temperatures greater than approximately one third of the absolute melting temperature. However, certain alloys exhibit viscoplasticity at room temperature (300K). For polymers, wood, and bitumen, the theory of viscoplasticity is required to describe behavior beyond the limit of elasticity or viscoelasticity.

In general, viscoplasticity theories are useful in areas such as

- the calculation of permanent deformations,
- the prediction of the plastic collapse of structures,
- the investigation of stability,
- crash simulations,
- systems exposed to high temperatures such as turbines in engines, e.g. a power plant,
- dynamic problems and systems exposed to high strain rates.

Phenomenology

For a qualitative analysis, several characteristic tests are performed to describe the phenomenology of viscoplastic materials. Some examples of these tests are

1. hardening tests at constant stress or strain rate,

2. creep tests at constant force, and
3. stress relaxation at constant elongation.

Strain hardening test

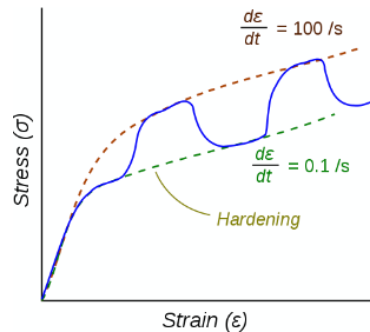


Figure 2. Stress–strain response of a viscoplastic material at different strain rates.

The dotted lines show the response if the strain-rate is held constant. The blue line shows the response when the strain rate is changed suddenly.

One consequence of yielding is that as plastic deformation proceeds, an increase in stress is required to produce additional strain. This phenomenon is known as Strain/Work hardening. For a viscoplastic material the hardening curves are not significantly different from those of rate-independent plastic material. Nevertheless, three essential differences can be observed.

1. At the same strain, the higher the rate of strain the higher the stress.
2. A change in the rate of strain during the test results in an immediate change in the stress–strain curve.
3. The concept of a plastic yield limit is no longer strictly applicable.

The hypothesis of partitioning the strains by decoupling the elastic and plastic parts is still applicable where the strains are small, i.e.,

$$\epsilon = \epsilon_e + \epsilon_{vp}$$

where ϵ_e is the elastic strain and ϵ_{vp} is the viscoplastic strain.

To obtain the stress–strain behavior shown in blue in the figure, the material is initially loaded at a strain rate of 0.1/s. The strain rate is then instantaneously raised to 100/s and held constant at that value for some time. At

the end of that time period the strain rate is dropped instantaneously back to 0.1/s and the cycle is continued for increasing values of strain. There is clearly a lag between the strain-rate change and the stress response. This lag is modeled quite accurately by overstress models (such as the Perzyna model) but not by models of rate-independent plasticity that have a rate-dependent yield stress.”

2.3 Metabolism index (MI) model

This model was developed in Y2014 by the author using the topology concept, nonlinear algebra, geometric algebra, and engineering finite element method. In summary, the human body metabolism is a complex mathematical problem with a matrix format of m causes by n symptoms, plus sometimes, one symptom or many symptoms would be turned into causes of another symptom.

This MI model contains 10 specific categories, including 4 output categories of medical conditions (body weight, glucose, blood pressure, and lipids), and 6 input categories of lifestyle details (food quantity and quality, drinking water intake, physical exercise, sleep, stress, and daily life routines). These 10 categories are comprised of approximately 500 detailed elements. He has also defined two new resulting parameters: the metabolism index or MI, as the combined score of the above 10 metabolism categories and 500 elements using his developed algorithm, along with the general health status unit (GHSU), as the 90-day moving average value of MI.

A physical analogy of this complex mathematical metabolism model is similar to “using multiple nails that are encircled by many rubber bands”. For example, at first, we hammer 10 nails into a piece of flat wood with an initial shape of a circle, then take 3,628,800 ($=10!$) rubber bands to encircle the nails, including all 10 nails. These ~3.6 million rubber bands (i.e. big number of relationships) indicate the possible relationships existing among these 10 nails (i.e. 10 original metabolism data). Some rubber bands encircle 2 nails or 3 nails and so on until the last rubber band encircles all of these 10 nails together (no rubber band to encircle a single nail is allowed). Now, if we move any one of the nails outward (i.e., moving away from the center of the nail

circle), then this moving action would create some internal tension inside the encircled rubber band. Moving one nail “outward” means one of these ten metabolism categories is becoming “unhealthy” which would cause some stress to our body. Of course, we can also move some or all of the 10 nails outward at the same time, but with different moving scales. If we can measure the summation of the internal tension created in the affected rubber bands, then this summarized tension force is equivalent to the metabolism value of human health. The higher tension means a higher metabolism value which creates an unhealthy situation. The author uses the above-described scenario of moving nails and their encircled rubber bands to explain his developed mathematical metabolism model of human health.

During 2010 and 2011, the author collected sparse biomarker data, but from the beginning of 2012, he has been gathering his body weight and finger-piercing glucose values each day. More complete data collection started in Y2015. In addition, he accumulates medical conditions data including BP, heart rate (HR), and blood lipids along with lifestyle details (LD). Since 2020, he has added the daily body temperature (BT) and blood oxygen level (SPO2) due to his concerns about being exposed to COVID-19. Based on the collected big data of biomarkers, he further organized them into two main groups. The first is the medical conditions group (MC) with 4 categories: weight, glucose, BP, and blood lipids. The second is the lifestyle details group (LD) with 6 categories: food & diet, exercise, water intake, sleep, stress, and daily routines. At first, he calculated a unique combined daily score for each of the 10 categories within the MC and LD groups. The combined scores of the 2 groups, 10 categories, and 500+ detailed elements constitute an overall “metabolism index (MI) model”. It includes the root causes of 6 major lifestyle inputs and symptoms from 4 lifestyle induced rudimentary chronic diseases, i.e. obesity, diabetes, hypertension, and hyperlipidemia. Therefore, the MI model, especially its 4 chronic disease conditions, can be used as the foundation and building block for his additional research work that can expand into various complications associated with different organs, such as cancer.

Of course, the same methodology can be extended to the study of many other medical complications, such as various heart problems (CVD & CHD), stroke, neuropathy, hypothyroidism, diabetic constipation, diabetic skin fungal infection, various cancers, and dementia.

In general, some genetic conditions and lifetime unhealthy habits, which include tobacco smoking, alcohol drinking, and illicit drug use, account for approximately 15% to 25% of the root-cause of chronic diseases and their complications, as well as cancers and dementia.

His calculated risk probability % for CKD, CVD, DR, stroke, and various cancers have some differences in their root-cause variables, their associated weighting factors for each key cause, and certain biomedical interpretations and assumptions. Specifically, the CVD/Stroke risk includes two major scenarios that combine emphasized weighting factors, blood vessel blockage due to blood glucose and blood lipids, and blood vessel rupture caused by blood glucose and blood pressure. Some recent research work have identified the relationship between pancreatic cancer with hyperglycemia and insulin resistance phenomena of type 2 diabetes, and chronic inflammation. Some aggressive prostate cancers are linked with 5 types of bacteria. There is also an evidence of a relationship between BP and DR (Reference: BP control and DR, by R. Klein and BEK Klein from British Journal of Ophthalmology). The CKD risks include hyperglycemic damage to micro-blood vessels and nerves which causes protein leakage found in urine and waste deposit within the kidneys; therefore, it requires dialysis to remove waste products and excess fluids from the body. However, the cancer risk also consists of additional influences from environmental conditions, such as some improper medications, viral infections, food pollution or poison, toxic chemical, radiation, air and water pollution, hormonal treatment, etc.

All of the above-mentioned diseases fall into the category of “symptoms” which are the outcomes of “root-causes” of genetic conditions, unhealthy lifestyles, and poor living environments.

Note: For a more detailed description, please refer to the “consolidated method” section which is given at the beginning of the special issue.

3. RESULTS

Figure 1 shows the stress-strain diagram of kidney cancer risk % with 4 hysteresis loops via a VGT energy analysis in a space domain.

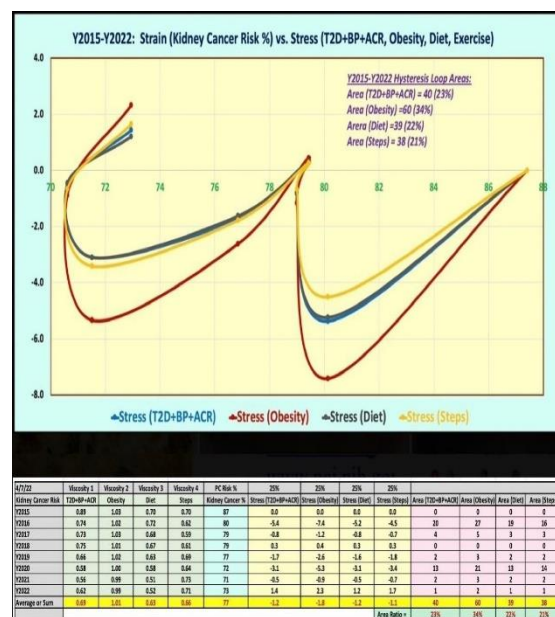


Figure 1: Stress-strain diagram of kidney cancer risk % with 4 hysteresis loops via VGT analysis in a space-domain.

4. CONCLUSION

The following four described biophysical characteristics have demonstrated certain behaviors of the author’s kidney cancer risk probability under 4 specific influential factors, using the viscoelastic or viscoplastic energy (VGT) approach:

- (1) From the x-axis value or the strain value on the stress-strain diagram, his kidney cancer risk % covers a range from the high-end of 87% in 2015 to the low-end of 73% in 2022. These kidney cancer risks are only relative numbers, not absolute numbers. However, on a relative scale, the reduction of his kidney cancer risk has not been as significant as the other types of cancer risks due to his long-term diabetic damage to his kidneys. Nevertheless, he feels at ease that his kidney cancer risks are decreasing.
- (2) From the y-axis (stress) values and the hysteresis loop areas, we can see that both the stress values and the hysteresis loop

areas for the period of Y2015-Y2018 are larger than the period of Y2019-Y2022. This indicates that, from the perspective of kidney cancer risk, he is “healthier” during the recent 4 years; therefore, his kidney cancer risks have been reduced accordingly due to the improvements made on his four influential factors, especially for factors of T2D+BP+ACR (disease biomarkers) and diet (food quality and quantity). On contrary, both obesity (body weight) and exercise (walking steps) are more and less remaining at constant levels.

(3) Based on the comparison of hysteresis loop area size or degrees of influence, the summarized sub-area of 96 (54%) for the earlier 4 years of Y2015-Y2018 is somewhat larger than the summarized sub-area of 81 (46%) for the recent 4 years of Y2019-Y2022. His stringent lifestyle management program initiated in Y2014 has indeed changed his risk perspective of having kidney cancer.

(4) When he delved deeper into the comparisons among these four influential factors, he can further identify some additional details regarding these “efforts and results” from each influential factor. Examples of the detailed observations are: obesity (body weight) contributes the most of 34% of the influence on his kidney cancer risk; the contributions from the other three influential factors are very close to each other with an order of T2D+BP+ACR of 23%, diet of 22%, and exercise of 21%.

In summary, conclusions 1 and 2 can also be observed from time-domain waveforms. However, conclusions 3 and 4 regarding energies and degrees of influence associated with risk factors can not be identified using time-domain curves. More importantly, the unique “time-dependency” character of strain change rate (i.e. cancer risk change amount over time) can only be presented via the VGT tool.

This kidney cancer risk article has demonstrated how the author utilizes the physics and engineering, VGT energy methodology, to construct and display the research result findings of his risk perspective of developing kidney cancer resulting from four interrelated influential factors.

5. REFERENCES

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

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Viscoelastic and Viscoplastic Glucose Theory Application in Medicine

Gerald C. Hsu

