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The GH-Method

Viscoelastic or Viscoplastic Glucose Theory (VGT #61): A Simplified Mathematical Model to Estimate Pancreatic Cancer (PC) Risk Probability Percentages and its Moving Trend Over an ~7 Years Period from Y2015 to Y2022 Using Hyperglycemia, Insulin Resistance, Obesity, Chronic Inflammation, and Metabolism Index as the PC Risk's 5 Contribution Factors Based on GH-Method: Math-Physical Medicine (No. 649)

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Note: Readers who want to get a quick overview can read the abstract, results, and graphs.

Abstract

Recently, the author read a few published medical articles regarding pancreatic cancer (PC) and will outline some key information in the Introduction section. "Insulin resistance is an interrupted state in the biological response to insulin. It is reported that chronic hyperinsulinemia is associated with various types of cancer such as colorectal cancer, pancreatic cancer, endometrial cancer, and breast cancer (Reference 1). Symptoms of Insulin Resistance: Some signs of insulin resistance include a waistline over 40 inches in men and 35 inches in women; blood pressure readings of 130/80 or higher; and fasting glucose level over 100 mg/dL (Reference 2). (Note from the author: he had all of the above biomarker readings in 2010.) PC is a common cause of cancer-related death, due to difficulties in detecting early-stage disease, its aggressive behavior, and poor response to systemic therapy. Therefore, developing strategies for early diagnosis of resectable PC is critical for improving survival. Diabetes mellitus is another major public health problem worldwide. Furthermore, diabetes can represent both a risk factor and a consequence of PC: nowadays, the relationship between these two diseases is considered a high priority for research (Reference 3). Since its initial recognition in the 20th century, Pancreatic Cancer has always been considered a virtually incurable disease; likewise, the prognosis has not changed much in recent years, compounded by a worldwide increase in incidence [1,2]. Pancreatic Ductal Adenocarcinoma (PDAC) is the most common malignancy of the exocrine pancreas, accounting for > 90% of cases, with a very poor prognosis. In this review, we will focus exclusively on PDAC. Increasing evidence indicates the presence of a pathological link between obesity, diabetes, and PDAC (Reference 4). The incidence of obesity and type 2 diabetes (T2DM) in the Western world has increased dramatically in recent decades. According to the American Cancer Society, pancreatic cancer (PC) is the fourth leading cause of cancer-related death in the United States. The relationship between obesity, T2DM, and PC is complex. Due to an increase in obesity, diabetes, alcohol consumption, and sedentary lifestyle, the mortality due to PC is expected to rise significantly by the year 2040. The underlying mechanisms by which diabetes and obesity contribute to pancreatic tumorigenesis are not well understood. Furthermore, metabolism and microenvironment within the pancreas can also modulate pancreatic carcinogenesis. The risk of PC on a population level may be reduced by modifiable lifestyle risk factors. In this review, the interactions of diabetes and obesity to PC development were summarized, and novel strategies for the prevention and treatment of diabetes and PC were discussed. INTRODUCTION: PC is one of the ten most common cancers in humans. Most of the cases are pancreatic exocrine cancer, only 1%-2% of cases of PC are neuroendocrine tumors. According to the American Cancer Society, the incidence of PC was 53,770 in 2019, with an 85% concomitant mortality rate of 45,750 (23,800 men and 21,950 women). It is the fourth cause of cancer-related death in both men and women in the United States each year. In the United States, the number of new cases of PC was 12.4 per 100 000 men and women per year based on 2009-2013 cases. Despite massive effort on diagnosis and treatment, the 5-

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year survival rate has been increased to a mere 8%. By 2030, the number of deaths from PC will surpass breast, prostate, and colon cancer and become the second leading cause of cancer-related death in the United States. Due to unclear symptoms and no screening recommendations, a vast majority of PC patients are diagnosed at late stages, with already advanced disease and no opportunity for surgical intervention. The risk factors for PC include tobacco products, obesity, diabetes, chronic pancreatitis, alcohol abuse, malnutrition, hereditary conditions, and family history (Figure 1). Diabetes mellitus (DM), or impaired glucose tolerance, is concurrently present in 50%-80% of patients with PC. DM is a known risk factor for PC, and new-onset DM could be an early manifestation of PC, resulting from insulin resistance induced by a paraneoplastic syndrome or pancreatic ß-cell dysfunction. In addition, it has been demonstrated that moderate alcohol consumption had an insignificant impact, while high alcohol intake was associated with an increased risk of PC. Although the effects of DM and alcohol abuse on the development of PC have been studied for the last few decades, their molecular mechanisms of action are not well understood. We conducted this review to update and summarize the mechanisms of association among diabetes mellitus, obesity, alcoholism, other factors, and cancerous pancreas. In addition, prevention and treatment strategies are also critically discussed in this review paper (Reference 5). Background & Aims: Of subjects with new-onset diabetes (based on glycemia) over the age of 50 years, approximately 1% are diagnosed with pancreatic cancer within 3 years. We aimed to develop and validate a model to determine the risk of pancreatic cancer in individuals with new-onset diabetes. Based on the change in weight, change in blood glucose, and age at the onset of diabetes, we developed and validated a model to determine the risk of pancreatic cancer in patients with new-onset diabetes, based on glycemia (the END-PAC model) (Reference 6). Abstract - Background: Type 2 diabetes mellitus has been associated with an excess risk of PC, but the magnitude of the risk and the time-risk relationship is unclear, and there is limited information on the role of anti-diabetic medications. Results: Overall, 1,155 (15%) cases and 1,087 (8%) controls reported a diagnosis of T2D or more years before cancer diagnosis (or interview, for controls), corresponding to an OR of 1.90 (95% confidence interval, CI, 1.72-2.09). Consistent risk estimates were observed across strata of selected covariates, including body mass index and tobacco smoking. Pancreatic cancer risk decreased with the duration of diabetes, but a significant excess risk was still evident 20 or more years after diabetes diagnosis (OR 1.30, 95% CI 1.03-1.63). Among diabetics, a long duration of oral antidiabetic use was associated with a decreased pancreatic cancer risk (OR 0.31, 95% CI 0.14-0.69, for ≥15 years). Conversely, insulin use was associated with pancreatic cancer risk in the short term (OR 5.60, 95% CI 3.75-8.35, for <5 years), but not for a longer duration of use (OR 0.95, 95% CI 0.53-1.70, for ≥15 years). Conclusion: This study provides the most definitive quantification to date of excess risk of pancreatic cancer among diabetics. It also shows that a 30% excess risk persists for more than two decades after diabetes diagnosis, thus supporting a causal role of diabetes in pancreatic cancer. Oral antidiabetics may decrease the risk of pancreatic cancer, whereas insulin showed an inconsistent duration-risk relationship (Reference 7). Abstract - This study investigated the effects of diabetes and antidiabetic medications on the risk of pancreatic cancer (PaC). We extracted data on Koreans with newly diagnosed diabetes and selected age- and sex-matched controls provided by the National Health Insurance Corporation. Incident PaC was defined as a new registration in the Korea Central Cancer Registry under ICD-10 C25 with an admission history until 2015. During 19,429,617.1 person-years, 8,589 PaCs were identified in 1,005,409 subjects for diabetes group and 4,021,636 subjects for control group. The diabetes group showed more than a two-fold risk for PaC compared with the control group. Among antidiabetic medications, metformin, thiazolidinedione, and dipeptidyl peptidase-4 inhibitor exposure was associated with decreased risk for future PaC (hazard ratio[95% confidence interval] = 0.86[0.77–0.96], 0.82[0.68–0.98], 0.57[0.51–0.64], respectively), whereas sulfonylurea and insulin exposure was related to increased risk (hazard ratio[95% CI] = 1.73[1.57–1.91], 2.86[1.43–5.74], respectively) compared to subjects with no drug exposure. Moreover, subjects with dual exposure history to metformin plus thiazolidinedione or metformin plus dipeptidyl peptidase-4 inhibitor had a lower risk of PaC compared to metformin-only treated subjects. In conclusion, Korean adults with diabetes are at higher risk of PaC compared with nondiabetic individuals, and this risk may be modified by antidiabetic medications. To the best of our knowledge, this is the largest nationwide population-based cohort study that has shown an increased risk of incident PaC in diabetes patients regardless of age, sex, and observation period. In this study, not only metformin but also DPP4i or TZD exposure was associated with decreased risk of future PaC, whereas sulfonylurea or insulin exposure increased the risk. In addition, subjects with dual exposure to metformin plus TZD or metformin plus DPP4i were at lower risk of PaC compared with metformin-only treated subjects (Reference 8)". Based on those 8 referenced papers in this article, it is evident that the risk of having PC is related to T2D's insulin resistance and its associated hyperglycemic situations, obesity or overweight (BMI above 30 or over 25), chronic inflammation, and diabetic medications. Of course, similar to other types of cancers, the genetic conditions, family histories, lifetime unhealthy habits (alcohol drinking, cigarette

smoking, and illicit drug usage), and environmental influences (viral infections, food pollution or poison, toxic chemical, radiation, air and water pollution, hormonal treatment, and improper medications) play certain roles in the PC development as well. To simplify the complex root causes versus symptoms of PC, the author selects the following 5 root causes for assessing the author's PC risk %, i.e. hyperglycemia (or HyperG, from PPG above 180 mg/dL), insulin resistance (IR from FPG), obesity (body weight > 204 lbs for BMI >30 or weight > 170 lbs for BMI >25), chronic inflammation, and unhealthy metabolism index (or MI >73.5%). Furthermore, he has established a simple linear equation for estimating his PIC risk % as follows: PC risk % = hyperglycemia score * 0.15 + IR score * 0.15 + body weight * 0.15 + inflammation score * 0.15 + metabolism index * 0.4, where the hyperglycemic score is (average high PPG > 180 mg/dL divided by averaged PPG) * (number of meals having PPG > 180 mg/dL divided by the total number of meals); insulin resistance is measured by FPG in the early morning since there are no contributions to glucose by either food or exercise, except for the fundamental pancreatic beta cells insulin production capacity and capability; MI score will be described in the method section, and his chronic inflammation score is zero since he has no known chronic inflammation conditions. Since he is conducting a study to estimate his PC risk probability percentage over an ~7 years period from 1/1/2015 to 4/12/2022 by utilizing the collected data of his own body starting on 1/1/2012; therefore, it is necessary to provide a brief description of his health history. The author 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, along with 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 start insulin injections and kidney dialysis immediately. This was his wake-up call. He then decided to save his life by conducting his self-study and research on subjects of food nutrition and internal medicine, especially 4 metabolic induced chronic diseases that same year. His health profile in 2010 was: body weight at 220 lbs., average glucose at 280 mg/dL, FPG in the early morning at 180 mg/dL, lab-tested A1C 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. During the past 13 years, he has made significant lifestyle changes. For example, he consumes less than 20 grams of carbohydrates and sugar per meal, reduces his food quantity by 50%, avoids eating processed food, walks 6-7 miles or 10-11 kilometers daily, sleeps 7-8 hours each night, and avoids stress as much as possible. As of April 10, 2022, his health profile for the first 3 months of 2022 is body weight at 169 lbs., 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 is that he has ceased taking 3 different kinds of diabetes medications since 12/8/2015. Fortunately, he has not detected any sign of cancer to date. In summary, the following four described biophysical characteristics have demonstrated certain key behaviors of this pancreatic cancer risk using the VGT approach: (1) From the display of 5 input causes in a time domain (TD), insulin resistance has maintained a level around 4.5 with a small declination % year after year (from 5.0 at Y2015 to 3.9 at Y2022 which gives a 22% improvement over 7 years or ~3% reduction each year which means he has been self-repairing his damaged pancreatic beta cells at an annual rate of 3%). This observation is due to the long lifespan of pancreatic beta cells; therefore, the self-repair rate of damaged beta cells is very slow. His hyperglycemic (PPG >180 mg/dL) improvement is obvious from this figure which is the direct result of his stringent and persistent lifestyle management. He has also reduced his weight continuously from 220 lbs. (BMI 32) in Y2010 through 175 lbs. (BMI 25.8) in Y2015 and then down to 169 lbs. (BMI 24.95) in Y2022. As a result, within this selected 7 years timespan, he has not suffered from "obesity". As mentioned before, he does not have any records of chronic inflammation. (2) From the stress-strain hysteresis loops of VGT analysis in a space domain (SD), the right half of the triangular curves (Y2015-Y2017) have close proximity between hyperglycemia (HyperG) and insulin resistance (IR) which can also be observed from the TD curves. However, the left half of the triangular curves (Y2018-Y2022) have a large gap between hyperglycemia (HyperG) and insulin resistance (IR) but with proximity between hyperglycemia and obesity that can be seen from the TD curves. (3) The hysteresis loop areas are 112 for hyperglycemia, 309 for insulin resistance, and 68 for obesity. These data provide an area ratio of 1 : 1.6 : 4.5 for Hyperglycemia : IR : Obesity. It shows that his control effort on his weight and glucose are excellent while his IR improvement would take a longer time to see more significant improvement. Insulin resistance (IR) is a prominent biomarker for both pancreatic health conditions and chronic kidney diseases (CKD). In his personal opinion, pancreatic beta-cell damage may not be totally curable, but it is definitely self-repairable to a significant degree via lifestyle improvements. (4) His pancreatic cancer risk % (strain) was at a relative 33% in Y2015 and continuously decreased to a 15% level in Y2021 and 19% level in Y2022 (based only on 3+ months of Y2022 data). This observation indicates that his PC risk % is most likely between low and moderate risk levels and trending toward the lower-risk level through his stringent lifestyle management

program. In summary, conclusions 1 and 4 can also be observed from time-domain waveforms. However, conclusions 2 and 3 regarding energies and degrees of influence associated with cancer 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 pancreatic 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 pancreatic cancer resulting from three interrelated influential factors.

Keywords: Viscoelastic; Viscoplastic; Pancreatic cancer; Hyperglycemia; Insulin resistance; Obesity; Chronic inflammation; Metabolism index; Fasting plasma glucose; Postprandial plasma glucose; HbA1C

Abbreviations: PC: pancreatic cancer; PDAC: pancreatic ductal adenocarcinoma; T2DM: type 2 diabetes; 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 pancreatic cancer (PC) and will outline some key information in the Introduction section.

"Insulin resistance is an interrupted state in the biological response to insulin. It is reported that chronic hyperinsulinemia is associated with various types of cancer such as colorectal cancer, pancreatic cancer, endometrial cancer, and breast cancer (Reference 1).

Symptoms of Insulin Resistance:
Some signs of insulin resistance include a waistline over 40 inches in men and 35 inches in women; blood pressure readings of 130/80 or higher; and fasting glucose level over 100 mg/dL (Reference 2). (Note from the author: he had all of the above biomarker readings in 2010.)

PC is a common cause of cancer-related death, due to difficulties in detecting early-stage disease, its aggressive behavior, and poor response to systemic therapy. Therefore, developing strategies for early diagnosis of resectable PC is critical for improving survival. Diabetes mellitus is another major public health problem worldwide. Furthermore, diabetes can represent both a risk factor and a consequence of PC: nowadays, the relationship between these two diseases is considered a high priority for research (Reference 3).

Since its initial recognition in the 20th century, Pancreatic Cancer has always been considered a virtually incurable disease; likewise, the prognosis has not changed much in recent years, compounded by a worldwide increase in incidence [1,2]. Pancreatic Ductal Adenocarcinoma (PDAC) is the most common malignancy of the exocrine pancreas, accounting for > 90% of cases, with a very poor prognosis. In this review, we will focus exclusively on PDAC. Increasing evidence indicates the presence of a pathological link between obesity, diabetes and PDAC (Reference 4).

The incidence of obesity and type 2 diabetes (T2DM) in the Western world has increased dramatically in recent decades. According to the American Cancer Society, pancreatic cancer (PC) is the fourth leading cause of cancer-related death in the United States. The relationship between obesity, T2DM, and PC is complex. Due to an increase in obesity, diabetes, alcohol consumption, and sedentary lifestyle, the mortality due to PC is expected to rise significantly by the year 2040. The underlying mechanisms by which diabetes and obesity contribute to pancreatic tumorigenesis are not well understood. Furthermore, metabolism and microenvironment within the pancreas can also modulate pancreatic carcinogenesis. The risk of PC on a population level may be reduced by modifiable lifestyle risk factors. In this review, the interactions of diabetes and obesity to PC development were summarized, and novel strategies for the prevention and treatment of diabetes and PC were discussed.

INTRODUCTION
PC is one of the ten most common cancers in humans. Most of the cases are pancreatic exocrine cancer, only 1%-2% of cases of PC are neuroendocrine tumors. According to the American Cancer Society, the incidence of PC was 53,770 in 2019, with an 85% concomitant mortality rate of 45,750 (23,800 men and 21,950 women). It is the fourth cause of cancer-related death in both men and women in the United States each year. In the United States, the number of new cases of PC was 12.4 per 100 000 men and women per year based on 2009-2013 cases. Despite massive effort on diagnosis and treatment, the 5-year survival rate has been increased to a mere 8%. By 2030, the number of deaths from PC will surpass breast, prostate, and colon cancer and become the second leading cause of cancer-related death in the United States. Due to unclear symptoms and no screening recommendations, a vast majority of PC patients are diagnosed at late stages, with already advanced disease and no opportunity for surgical intervention. The risk factors for PC include tobacco products, obesity, diabetes, chronic pancreatitis, alcohol abuse, malnutrition, hereditary conditions, and family history (Figure 1). Diabetes mellitus (DM), or impaired glucose tolerance, is concurrently present in 50%-80% of patients with PC. DM is a known risk factor for PC, and new-onset DM could be an early manifestation of PC, resulting from insulin resistance induced by a paraneoplastic syndrome or pancreatic ß-cell dysfunction. In

addition, it has been demonstrated that moderate alcohol consumption had an insignificant impact, while high alcohol intake was associated with an increased risk of PC. Although the effects of DM and alcohol abuse on the development of PC have been studied for the last few decades, their molecular mechanisms of action are not well understood. We conducted this review to update and summarize the mechanisms of association among diabetes mellitus, obesity, alcoholism, other factors, and cancerous pancreas. In addition, prevention and treatment strategies are also critically discussed in this review paper (Reference 5).

Background & Aims
Of subjects with new-onset diabetes (based on glycemia) over the age of 50 years, approximately 1% are diagnosed with pancreatic cancer within 3 years. We aimed to develop and validate a model to determine the risk of pancreatic cancer in individuals with new-onset diabetes.

Based on the change in weight, change in blood glucose, and age at the onset of diabetes, we developed and validated a model to determine the risk of pancreatic cancer in patients with new-onset diabetes, based on glycemia (the END-PAC model) (Reference 6).

Abstract
Background: Type 2 diabetes mellitus has been associated with an excess risk of PC, but the magnitude of the risk and the time-risk relationship is unclear, and there is limited information on the role of anti-diabetic medications.

Results: Overall, 1,155 (15%) cases and 1,087 (8%) controls reported a diagnosis of T2D or more years before cancer diagnosis (or interview, for controls), corresponding to an OR of 1.90 (95% confidence interval, CI, 1.72-2.09). Consistent risk estimates were observed across strata of selected covariates, including body mass index and tobacco smoking. Pancreatic cancer risk decreased with the duration of diabetes, but a significant excess risk was still evident 20 or more years after diabetes diagnosis (OR 1.30, 95% CI 1.03-1.63). Among diabetics, a long duration of oral antidiabetic use was associated with a decreased pancreatic cancer risk (OR 0.31, 95% CI 0.14-0.69, for ≥15 years). Conversely, insulin use was associated with pancreatic cancer risk in the short term (OR 5.60, 95% CI 3.75-8.35, for <5 years), but not for a longer duration of use (OR 0.95, 95% CI 0.53-1.70, for ≥15 years).

Conclusion: This study provides the most definitive quantification to date of excess risk of pancreatic cancer among diabetics. It also shows that a 30% excess risk persists for more than two decades after diabetes diagnosis, thus supporting a causal role of diabetes in pancreatic cancer. Oral antidiabetics may decrease the risk of pancreatic cancer, whereas insulin showed an inconsistent duration-risk relationship (Reference 7).

Abstract
This study investigated the effects of diabetes and antidiabetic medications on the risk of pancreatic cancer (PaC). We extracted data on Koreans with newly diagnosed diabetes and selected age- and sex-matched controls provided by the National Health Insurance Corporation. Incident PaC was defined as a new registration in the Korea Central Cancer Registry under ICD-10 C25 with an admission history until 2015. During 19,429,617.1 person-years, 8,589 PaCs were identified in 1,005,409 subjects for diabetes group and 4,021,636 subjects for control group. The diabetes group showed more than a two-fold risk for PaC compared with the control group. Among antidiabetic medications, metformin, thiazolidinedione, and dipeptidyl peptidase-4 inhibitor exposure was associated with decreased risk for future PaC (hazard ratio[95% confidence interval] = 0.86[0.77–0.96], 0.82[0.68–0.98], 0.57[0.51–0.64], respectively), whereas sulfonylurea and insulin exposure was related to increased risk (hazard ratio[95% CI] = 1.73[1.57–1.91], 2.86[1.43–5.74], respectively) compared to subjects with no drug exposure. Moreover, subjects with dual exposure history to metformin plus thiazolidinedione or metformin plus dipeptidyl peptidase-4 inhibitor had a lower risk of PaC compared to metformin-only treated subjects. In conclusion, Korean adults with diabetes are at higher risk of PaC compared with nondiabetic individuals, and this risk may be modified by antidiabetic medications.

To the best of our knowledge, this is the largest nationwide population-based cohort study that has shown an increased risk of

incident PaC in diabetes patients regardless of age, sex, and observation period. In this study, not only metformin but also DPP4i or TZD exposure was associated with decreased risk of future PaC, whereas sulfonylurea or insulin exposure increased the risk. In addition, subjects with dual exposure to metformin plus TZD or metformin plus DPP4i were at lower risk of PaC compared with metformin-only treated subjects (Reference 8)".

Based on those 8 referenced papers in this article, it is evident that the risk of having PC is related to T2D's insulin resistance and its associated hyperglycemic situations, obesity or overweight (BMI above 30 or over 25), chronic inflammation, and diabetic medications. Of course, similar to other types of cancers, the genetic conditions, family histories, lifetime unhealthy habits (alcohol drinking, cigarette smoking, and illicit drug usage), and environmental influences (viral infections, food pollution or poison, toxic chemical, radiation, air and water pollution, hormonal treatment, and improper medications) play certain roles in the PC development as well. To simplify the complex root causes versus symptoms of PC, the author selects the following 5 root causes for assessing the author's PC risk %: hyperglycemia (or HyperG, from PPG above 180 mg/dL), insulin resistance (IR from FPG), obesity (body weight > 204 lbs for BMI >30 or weight > 170 lbs for BMI >25), chronic inflammation, and unhealthy metabolism index (or MI >73.5%).

Furthermore, he has established a simple linear equation for estimating his PIC risk % as follows:

PC risk %
= hyperglycemia score * 0.15 + IR score * 0.15 + body weight * 0.15 + inflammation score * 0.15 + metabolism index * 0.4

Where the hyperglycemic score is (average high PPG > 180 mg/dL divided by averaged PPG) * (number of meals having PPG > 180 mg/dL divided by the total number of meals); insulin resistance is measured by FPG in the early morning since there are no contributions to glucose by either food or exercise, except for the fundamental pancreatic beta cells insulin production capacity and capability; MI score will be described in the Method section, and his chronic inflammation score is zero since he has no known chronic inflammation conditions.

Since he is conducting a study to estimate his PC risk probability percentage over an ~7 years period from 1/1/2015 to 4/12/2022 by utilizing the collected data of his own body starting on 1/1/2012; therefore, it is necessary to provide a brief description of his health history.

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During the past 13 years, he has made significant lifestyle changes. For example, he consumes less than 20 grams of carbohydrates and sugar per meal, reduces his food quantity by 50%, avoids eating processed food, walks 6-7 miles or 10-11 kilometers daily, sleeps 7-8 hours each night, and avoids stress as much as possible.

As of April 10, 2022, his health profile for the first 3 months of 2022 is body weight at 169 lbs., 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 is that he has ceased taking 3 different kinds of diabetes medications since 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 in the method section.

2.1 Relationships between biomedical causes and biomedical symptoms

As a mathematician/engineer and conducting his medical research work during 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 x 1, 1 x n, m x 1, or m x 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 similar to Reference 3 that diabetes can represent both a risk factor and a consequence of PC, which is 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. Over the past 13 years, 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 around 60 sets of input/output biomarkers. The purpose is to identify certain hidden relationships between certain output biomarkers, such as pancreatic cancer risk (PC risk), and its corresponding multiple inputs, such as hyperglycemia, insulin resistance, obesity, chronic inflammation, and metabolism index. 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. This important time-dependency characteristic provides insight on the PC risk's moving pattern. It also controls the 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 complication 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 (increasing glucose) and unloading (decreasing body weight) over the timespan of the PC risk %. He calls this relative energy the "VGT energy".

It should be emphasized here that both PC 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 causes)
= η * (dε/dt)
= η * (d-strain/d-time)
= (viscosity factor η using normalized cause at present time) * (symptom at present time - symptom at a previous time)

Where the strain is the PC risk percentage and the stress is his PC risk change rate multiplied by three preferred input biomarkers, hyperglycemia, insulin

resistance, and obesity, as the three selected viscosity factors. In the VGT studies, sometimes, he carefully selects certain normalization factors for individual input biomarkers, respectively. The normalization factors are the dividing lines between a healthy state and an unhealthy state. For example, 170 lbs. is for body weight, 120 mg/dL for glucose, 180 mg/dL for hyperglycemia, 6.0% for HbA1C, and 73.5% for MI.

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.

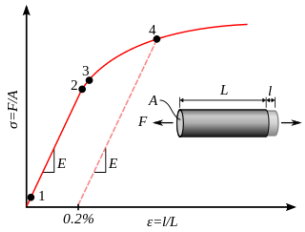
In engineering, the elasticity of a material is quantified by the elastic modulus such as the Young's modulus, bulk modulus or shear modulus which measure the amount of stress needed to achieve a unit of strain; a higher

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):

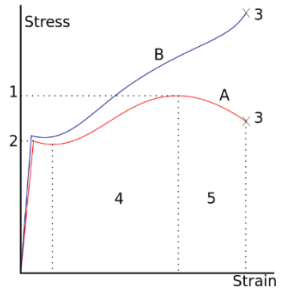
Deformation of a solid material undergoing non-reversible changes of shape in response to applied forces.

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/A0)
- 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 visco-plastically."

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).

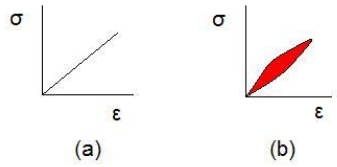
Depending on the change of strain rate versus stress inside a material, the viscosity can be categorized as having a linear, non-linear, or plastic response. When a material exhibits a linear response, it is categorized as a Newtonian material. In this case the stress is linearly proportional to the 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

$$\oint \sigma d\varepsilon$$

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.

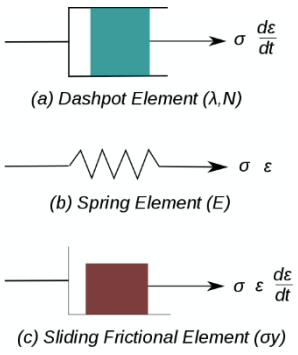


Figure 1. Elements used in one-dimensional models of viscoplastic materials.

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 [$\sigma(d\varepsilon/dt) = \sigma = \lambda(d\varepsilon/dt)(1/N)$]. The sliding element can have a yield stress (σy) 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

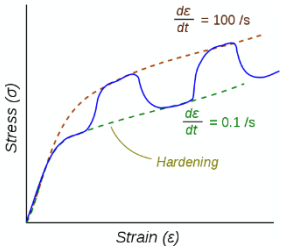


Figure 2. Stress–strain response of a viscoplastic material at different strain rates.

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.,

$\varepsilon = \varepsilon e + \varepsilon vp$

where εe is the elastic strain and εvp 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 Time-frequency analysis via fast Fourier transform

Time and frequency domain analysis of signals:

A Review by Getachew Admassie Ambaye, Faculty of Mechanical and Industrial Engineering, Bahir Dar Institute of Technology (BiT), Bahir Dar, Ethiopia.

The time domain is the analysis of mathematical functions, and physical signals with respect to time. In the time domain, the signal or function's value is known for all real numbers, in the case of continuous-time, or at various separate instants in the case of discrete-time. An oscilloscope is a tool commonly used to visualize real-world signals in the time domain. A time-domain graph shows how a signal changes with time, whereas a frequency-domain graph shows how much of the signal lies within each given frequency band over a range of frequencies. The frequency-domain refers to the analysis of mathematical functions or signals with respect to frequency, rather than time. Put simply, a time-domain graph shows how a signal changes over time, whereas a frequency-domain graph shows how much of the signal lies within each given frequency band over a range of frequencies. A frequency-domain representation can also include information on the phase shift that must be applied to each sinusoid to be able to recombine the frequency components to recover the original time signal. And finally, the time-frequency signal analysis was introduced, it's a new method in which the problem that had on the frequency signal analysis will be solved.

Time-frequency analysis

Techniques and methods in signal processing (from Wikipedia)

In signal processing, the time-frequency analysis comprises those techniques that study a signal in both the time and frequency domains simultaneously, using various time-frequency. Rather than viewing a 1-dimensional signal (a function, real or complex-valued, whose domain is the real line) and some transform (another function whose domain is the real line, obtained from the original via some transform), time-frequency analysis studies a two-dimensional signal – a function whose domain is the two-dimensional real plane, obtained from the signal via a time-frequency transform.

Fourier transform (from Wikipedia):

Mathematical transform that expresses a function of time as a function of frequency.

A Fourier transform (FT) is a mathematical transform that decomposes functions depending on space or time into functions depending on the spatial frequency or temporal frequency. An example application would be decomposing the waveform of a musical chord in terms of the intensity of its constituent pitches. The term Fourier transform refers to both the frequency domain representation and the mathematical operation that associates the frequency domain representation to a function of space or time.

2.4 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 has identified the relationship between pancreatic cancer with hyperglycemia and insulin resistance phenomena of T2D and chronic inflammation. Some aggressive prostate cancers are linked to 5 types of bacteria. There is also 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 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 5 contribution factors (causes) of PC risk in the time domain with a summary data table.

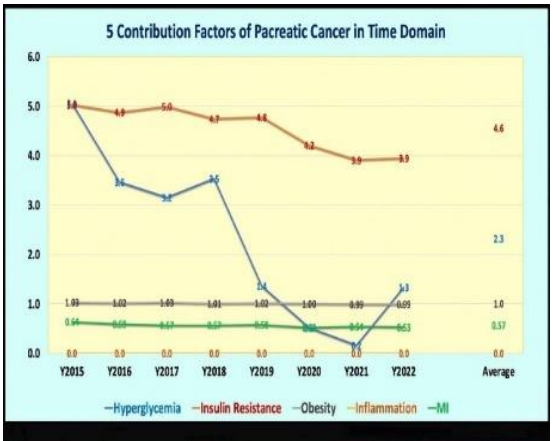
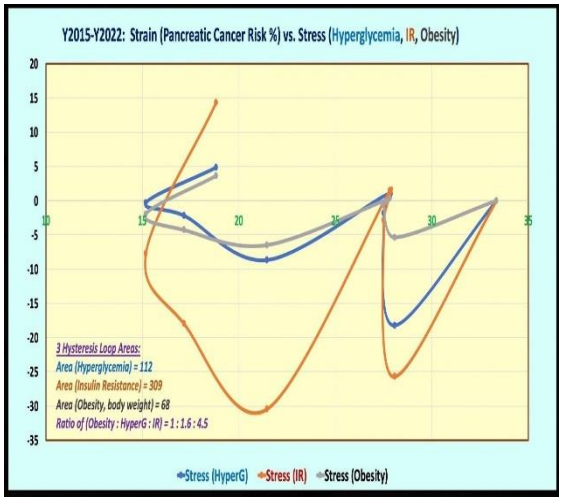


Figure 1: 5 contribution factors (causes) of PC risk in a time domain with summary data table.

Figure 2 displays the stress-strain diagram of 3 hysteresis loops via VGT analysis in the space domain with a data table.



4/7/22	Viscosity 1	Viscosity 2	Viscosity 3	PC Risk %						
PC Risk vs. HyperG & IR	HyperGlycemia	Insulin Resistance	Body Weight	Strain (PC Risk %)	Stress (HyperG)	Stress (IR)	Stress (Obesity)	Area (HyperG)	Area (IR)	Area Obesity)
Y2015	5.1	5.0	1.0	33	0	0	0	0	0	0
Y2016	3.5	4.9	1.0	28	-18	-26	-5	48	68	14
Y2017	3.2	5.0	1.0	28	-2	-3	-1	6	8	2
Y2018	3.5	4.7	1.0	28	1	2	0	0	0	0
Y2019	1.4	4.8	1.0	21	-9	-30	-6	24	92	20
Y2020	0.5	4.2	1.0	17	-2	-38	-4	23	104	23
Y2021	0.2	3.9	1.0	15	0	-8	-2	3	26	6
Y2022	1.3	3.9	1.0	19	5	14	4	8	12	3
Average or Sum	2.3	4.6	1.0	24	-3	-9	-2	112	309	68
					Stress Ratio =	37%	171%	Area Ratio =	36%	165%

Figure 2: Stress-strain diagram of 3 hysteresis loops via VGT analysis in a space domain with a data table.

4. CONCLUSION

In summary, the following four described biophysical characteristics have demonstrated certain key behaviors of this pancreatic cancer risk using the VGT approach:

(1) From the display of 5 input causes in a time domain (TD), insulin resistance has maintained a level around 4.5 with a small declination % year after year (from 5.0 at Y2015 to 3.9 at Y2022 which gives a 22% improvement over 7 years or ~3% reduction each year which means he has been self-repairing his damaged pancreatic beta cells at an annual rate of 3%). This observation is due to the long lifespan of pancreatic beta cells; therefore, the self-repair rate of damaged beta cells is very slow. His hyperglycemic (PPG >180 mg/dL) improvement is obvious from this figure which is the direct result of his stringent and persistent lifestyle management. He has also reduced his weight continuously from 220 lbs. (BMI 32) in Y2010 through 175 lbs. (BMI 25.8) in Y2015 and then down to 169 lbs. (BMI 24.95) in Y2022. As a result, within this selected 7-year time span, he has not suffered from "obesity". As mentioned before, he does not have any records of chronic inflammation.

(2) From the stress-strain hysteresis loops of VGT analysis in a space domain (SD), the right half of the triangular curves (Y2015-Y2017) have close proximity between hyperglycemia (HyperG) and insulin resistance (IR) which can also be observed from the TD curves. However, the left half of the triangular curves (Y2018-Y2022) have a large gap between hyperglycemia (HyperG) and insulin resistance (IR) but with proximity between hyperglycemia and obesity can be seen from the TD curves.

(3) The hysteresis loop areas are 112 for hyperglycemia, 309 for insulin resistance, and 68 for obesity. These data provide an area ratio of 1 : 1.6 : 4.5 for Hyperglycemia : IR : Obesity. It shows that his control effort on his weight and glucose are excellent while his IR improvement would take a longer time to see more significant improvement. Insulin resistance (IR) is a prominent biomarker for both pancreatic health conditions and chronic kidney diseases (CKD). In his personal opinion, pancreatic beta-cell damage may not be totally curable, but it is definitely self-repairable to a significant degree via lifestyle improvements.

(4) His pancreatic cancer risk % (strain) was at a relative 33% in Y2015 and continuously decreased to a 15% level in Y2021 and 19% level in Y2022 (based only on 3+ months of Y2022 data). This observation indicates that his PC risk % is most likely between low and moderate risk levels and trending toward the lower-risk level through his stringent lifestyle management program.

In summary, conclusions 1 and 4 can also be observed from time-domain waveforms. However, conclusions 2 and 3 regarding energies and degrees of influence associated with cancer 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 pancreatic 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 pancreatic cancer resulting from three 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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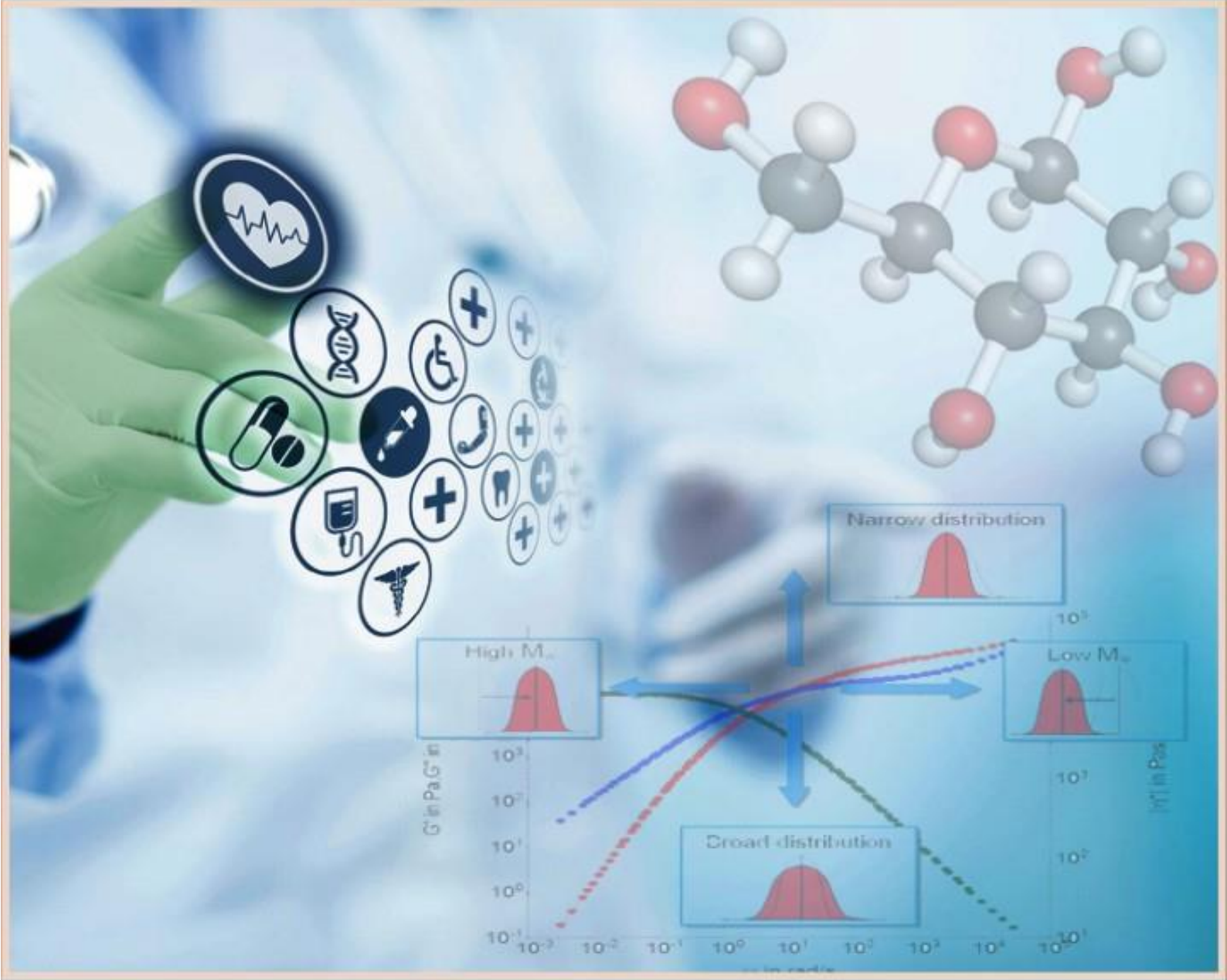
Special Issue | Issue No. 5 The GH-Method

Viscoelastic and Viscoplastic Glucose Theory Application in Medicine

Gerald C. Hsu



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