

# **HEALTH RISK ANALYSIS SYSTEM**

## **HEALTH RISK FACTORS DEFINED**

Scientifically validated and FDA cleared, this Class 2 analytical medical device performs a range of tests covered and reimbursed by most insurance carriers. The one-page Physician Dashboard provides a quick and comprehensive overview of a patient's health risks in a matter of seconds, thus allowing the Medical Professional to focus their attention more quickly toward more specific potential diagnoses.

#### 1 AUTONOMIC NERVOUS SYSTEM DYSFUNCTION RISK - ANSD

Problems with the ANS can range from mild to life threatening. Sometimes only one part of the nervous system is affected. In other cases, the entire ANS is affected. Some conditions are temporary and can be reversed, while others are chronic and will continue to worsen over time. Diseases such as Diabetes or Parkinson's disease can cause irregularities with the ANS. Problems with ANS regulation often involve organ failure, or the failure of the nerves to transmit a necessary signal.

#### 2 SUDOMOTOR DYSFUNCTION RISK - SudoD

Sudomotor dysfunction testing may indicate to physicians a patient's peripheral nerve and cardiac sympathetic dysfunction. Neuropathy is a common complication in diabetes mellitus (DM), with 60%-70% of patients affected over their lifetime. Symptoms of neuropathy are very common, and sub-clinical neuropathy is more common than clinical neuropathy. Neuropathy may remain undetected, and progress over time leading to serious complications. The most common associated clinical condition is peripheral neuropathy, affecting the feet. Autonomic nerve involvement is common but probably the most undiagnosed. Low scores in the sudomotor may lead a medical provider to look at clinical neuropathy.

#### 3 ENDOTHELIAL DYSFUNCTION RISK - EndoD

Current evidence suggests that endothelial function is an integrative marker of the net effects of damage from traditional and emerging risk factors on the arterial wall and its intrinsic capacity for repair. Endothelial dysfunction, detected as the presence of reduced vasodilating response to endothelial stimuli, has been observed to be associated with major cardiovascular risk factors, such as aging, hyperhomocysteinemia, post menopause state, smoking, diabetes, hypercholesterolemia, and hypertension.

#### **4 INSULIN RESISTANCE RISK – IR**

Insulin resistance is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population. Insulin resistance occurs as part of a cluster of cardiovascular metabolic abnormalities commonly referred to as "The Insulin Resistance Syndrome" or "The Metabolic Syndrome". This cluster of abnormalities may lead to the development of type 2 diabetes, accelerated atherosclerosis, hypertension or polycystic ovarian syndrome depending on the genetic background of the individual developing the insulin resistance.

#### 5 CARDIOMETABOLIC RISK - CMR

The specific factors that can cause this increased risk include: obesity (particularly central), hyperglycemia, hypertension, insulin resistance and dyslipoproteinemia. When patients have one or more risk factors and are physically inactive or smoke, the cardiometabolic risk is increased even more. Medical conditions that often share the above characteristics, such as type 2 diabetes, can also increase cardiometabolic risk. The primary focus of cardiometabolic risk treatment is management of each high risk factor, including dyslipoproteinemia, hypertension, and diabetes. The management of these subjects is based principally on lifestyle measures, but various antihypertensive, lipid-lowering, insulin sensitizing, anti-obesity and antiplatelet drugs could be helpful in reducing cardiometabolic risk.

#### **6 SMALL FIBER NEUROPATHY RISK – SFN**

A small fiber neuropathy occurs when damage to the peripheral nerves predominantly or entirely affects the small myelinated fibers or unmyelinated C fibers. The specific fiber types involved in this process include both small somatic and autonomic fibers. The sensory functions of these fibers include thermal perception and nociception. These fibers are involved in many autonomic and enteric functions.

#### 7 CARDIAC AUTONOMIC NEUROPATHY RISK – CAN

High blood glucose levels over a period of years may cause a condition called autonomic neuropathy. This is damage to the nerves that control the regulation of involuntary function. When the nerve damage affects the heart, it is called cardiac autonomic neuropathy (CAN). CAN encompasses damage to the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities in heart rate control, vascular dynamics and the body's ability to adjust blood pressure. CAN is a significant cause of morbidity and mortality associated with a high risk of cardiac arrhythmias and sudden death.

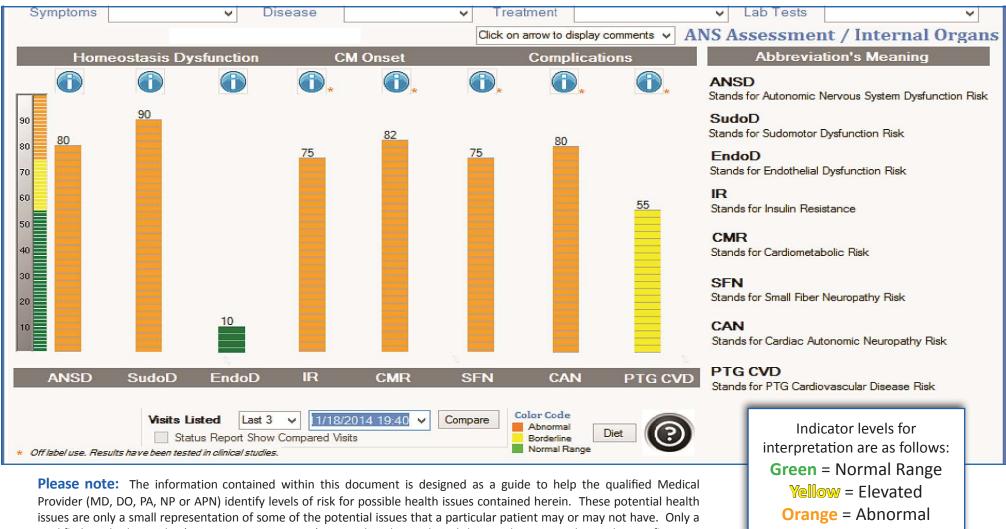
#### 8 PLETHYSMOGRAPHY CARDIOVASCULAR DISEASE RISK – PTG CVD

The PTG CVD risk factor is the combined total of the other seven risk factors assessments. It takes into consideration the cardiovascular as well as the autonomic nervous system (ANS) measurements.

## ANALYSIS DASHBOARD

### A Review of the 8 Key Risk Factors (Bar Graphs)

Page 1 of a sample Physician's Full Report Summary.

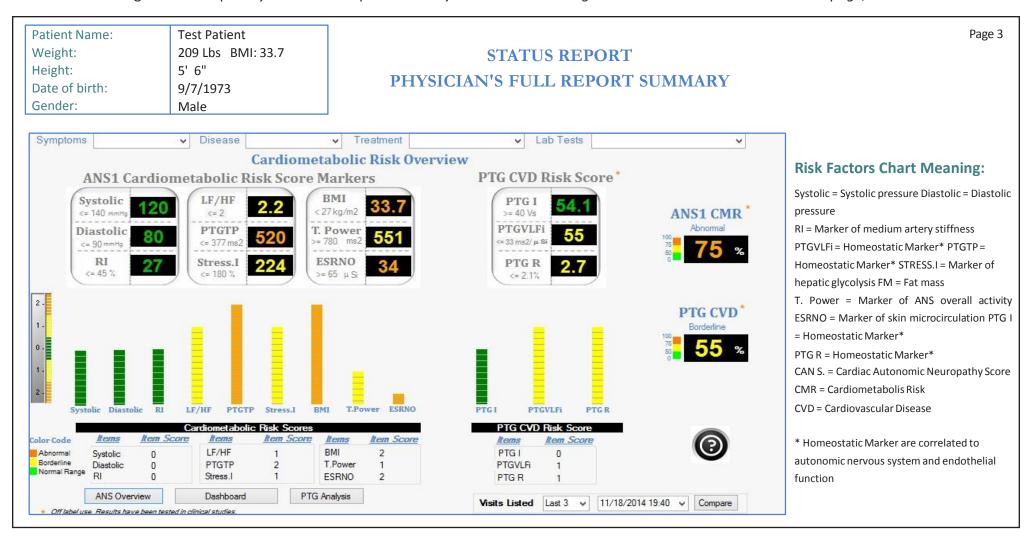


Please note: The information contained within this document is designed as a guide to help the qualified Medical Provider (MD, DO, PA, NP or APN) identify levels of risk for possible health issues contained herein. These potential health issues are only a small representation of some of the potential issues that a particular patient may or may not have. Only a qualified Medical Provider (MD, DO, PA, NP or APN) may utilize this analytical data to diagnose and provide specific treatment regimens for any health issue. We, any of our employees, agents and/or other affiliates do not claim to diagnose or to suggest in any way that any Medical Provider (MD, DO, PA, NP or APN) follow these examples for diagnosing a patient, unless the Medical Provider (MD, DO, PA, NP or APN) determines on his/her own behalf that any of these said health issues may or may not exist for each patient. This reference guide lists other additional testing that a Medical Provider (MD, DO, PA, NP or APN) might opt to have done for a patient. However, we do not in any way claim that these tests are the only tests available, are applicable for all patients, are necessary or should ever be run at all.

All decisions on testing and diagnosing remain the responsibility of a qualified Medical Provider (MD, DO, PA, NP or APN)

## **Autonomic Nervous System Dysfunction (ANSD)**

Page 3 of a sample Physician's Full Report Summary reveals ANSD through the Cardiometabolic Risk Overview page, below.



## **Autonomic Nervous System Dysfunction (ANSD)**

Correlates to the first Risk Factor Bar on the graph on Page 1 on Physician's Full Report Summary

#### **Possible Symptoms**

- Blurred Vision
- Elevated Blood Sugar
- Extreme Thirst
- Fatigue
- Frequent Urination
- Heartburn
- Increased Hunger
- Nausea
- Numbness & Tingling in Hands or Feet
- Vomiting

#### Possible Condition(s)

- Diabetes
- Cardiovascular Disease (CVD)
- Metabolic Disorders

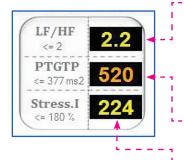
#### **Additional Testing**

(At physician's discretion)

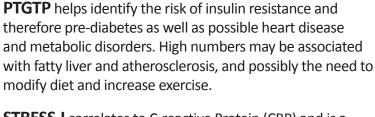
- Hemoglobin A1C
- Lipid Profile
- Complete Blood Count
- Cardiovascular Disease
- Insulin Resistance
- CMP (Complete Metabolic Profile)
- Ultrasound
- Ankle Brachial Index (ABI)

#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):

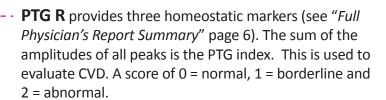


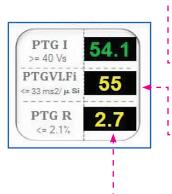
**LF/HF** indicates ANS balance. If the value is high (greater than 2), it indicates sympathetic system predominance and possibility of mental stress or anxiety. If the value is low (less than 0.5), it indicates parasympathetic system predominance and possibility of fatigue or depression. **PTGTP** below identify the risk of insulin resistance and



**STRESS.I** correlates to C-reactive Protein (CRP) and is a marker for sympathetic failure. High numbers indicate a risk for heart disease.

**PTGVLFi** is a marker for impaired glucose testing (IGT) and microcirculation complications. High numbers indicate a risk of diabetes.





## Sudomotor Dysfunction (SudoD) Page

7 of a sample Physician's Full Report Summary.

Patient Name: Test Patient
Weight: 209 Lbs BMI: 33.7
Height: 5' 6"
Date of birth: 9/7/1973
Gender: Male

## STATUS REPORT PHYSICIAN'S FULL REPORT SUMMARY

Page 7

Sudomotor Response (SMR) Analysis Conductance - Electrode Latency At Anode Conductance + Electrode Items N.Range Results Sudomotor Response Sudomotor Response Score 1230 🚍 3.10 1230 Significant Risk 1024 2.90 1024 2.70 896 896 768 2.50 768 2.42 Sudomotor Score 640 2.30 640 *Items* Items Score 512 2.10 512 **ESRNO** 2 ESR L 2 384 1.90 384 Peak C 256 1.70 Sudomotor responses analysis **ESRNO** ESR L Peak C 75 50 Abnormal Borderline 25 Normal Range 45 ANS Overview ANS Baseline ANS Tests Sudomotor Results Comments Moderate Microcirculation disorder Visits Listed Last 3 1/18/2014 19:40 Moderately reduced C-Fiber velocity Compare Moderately decreased sweat gland function

The health information provided by us is solely for informational purposes as a public service to promote consumer health. It is not meant to provide medical advice tailored in any way. It does not constitute medical advice and is not intended to be a substitute for proper medical care provided by a physician. We assume no responsibility for any circumstances arising out of the use, misuse, interpretation or application of any information supplied. It is the responsibility of the physician or medical Professional to diagnose and provide the appropriate examinations, treatment, testing, and care recommendations.

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## **Sudomotor Dysfunction (SudoD)**

Correlates to the second Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

- Burning Sensation
- Difficulty Digesting Food
- Dizziness or Fainting
- Exercise Intolerance
- Possible Microcirculation Issues
- Sexual Difficulties
- Sluggish Pupil Reaction
- Sweat Abnormalities
- Tingling Hands & Feet
- Urinary Problems

#### Possible Condition(s)

- Diabetes
- Cardiovascular Disease
- Peripheral & Distal Neuropathies

#### **Additional Testing**

(At physician's discretion)

- Breathing Test
- Gastrointestinal Testing (Gastric Emptying)
- QSART
- Urodynamic Testing (Bladder/Urinary Tract)
- Ultrasound

#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):



**ESRNO** is a marker of electrical skin response to nitric oxide (NO) production and vasodilation. This marker reflects microcirculation blood flow. Decreased ESR NO indicates microcirculation issues. Low numbers indicate signs of poor micro vascularization and increased risk of distal neuropathy.

**ESR L** is a marker of sweat gland nerve density. This marker reflects post sympathetic nerve density. The peak reflects C-fiber density. Low numbers are an early detection of peripheral distal neuropathy.

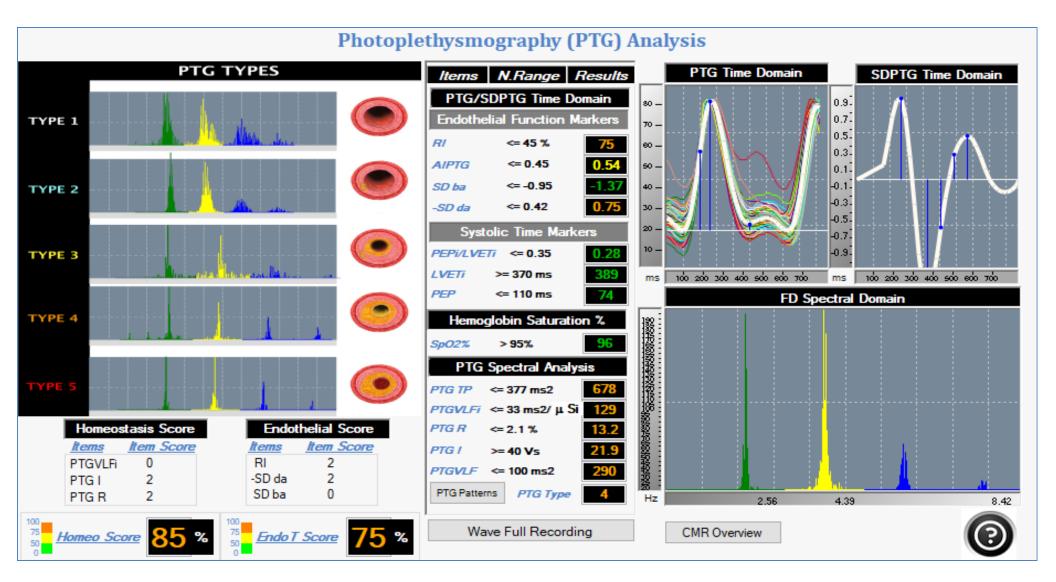
**Peak C** is a marker of sweat gland function and reflects maximum number of water and chlorine released on the electrode plate after stimulation. Decreased Peak C is either due to nerve damage or hypohidrosis (ie: low sweat). An abnormal number (high or low) can be attributed to hyperhidrosis (ie: excessive sweat). Low Peak C numbers are found with nerve damage.

Patient Name: Test Patient

Weight: 291 Lbs BMI: 33.7

Height: 5' 6"
Date of birth: 9/7/1973
Gender: Male

## STATUS REPORT PHYSICIAN'S FULL REPORT SUMMARY



## **Endothelial Dysfunction (EndoD)**

Correlates to the third Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

- Angina
- Cardiovascular Disease
- Chest Pain that Goes Away with Rest
- Heartburn
- Pain in Calves
- Stroke
- TIA

#### **Possible Condition(s)**

Endothelial Dysfunction (ANS Biomarker of Atherosclerosis)

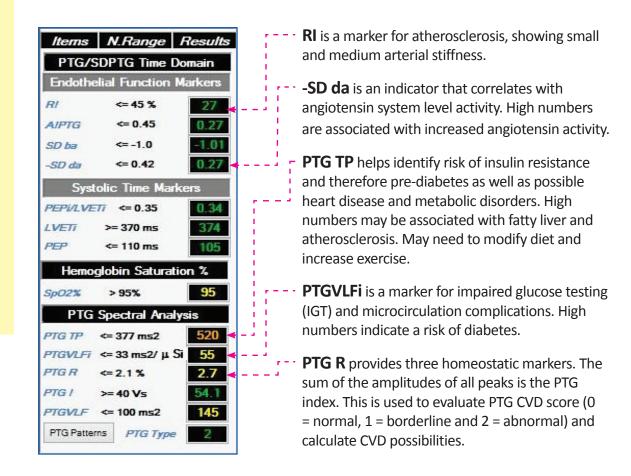
#### **Additional Testing**

(At physician's discretion)

- C-Reactive Protein (CRP)
- Stress Test
- Ultrasound
- Angiograph
- Ankle Brachial Index (ABI)

#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):



## **Insulin Resistance (IR)**

Page 1 of a sample Physician's Full Report Summary.

Patient Name: **Test Patient** Page 1 Weight: 209 Lbs BMI: 33.7 STATUS REPORT 5' 6" Height: PHYSICIAN'S FULL REPORT SUMMARY Date of birth: 9/7/1973 Gender: Male **Clinical Context** Comments And Suggestions Of The Risk Analysis ANSD: Moderate autonomic dysfunction detected. Possibility of mental stress. Increased physical activity is suggested. SudoD: Moderate Microcirculation disorder Moderately reduced C-Fiber velocity Moderately decreased sweat gland function EndoD: The result is in normal range. IR: Moderate Abnormal result. Lifestyle change is suggested. CMR: Moderate abnormal result. Further lab tests (Fasting BG and OGTT) are suggested **Observations** SFN: Moderate result. Further supplementary exams comprised in Toronto Clinical Neuropathy Score are suggested. CAN: Moderate Abnormal result. Significant failure of parasympathetic response. PTG CVD: Mild endothelial and ANS dysfunction detected. Cardiometabolic Profile lab tests are suggested. Symptoms Disease Treatment Lab Tests \*Off label use. Results have been tested in clinical studies. Click on arrow to display comments V ANS Assessment / Internal Organs Renua3A Dashboard Abbreviation's Meaning CM Onset Homeostasis Dysfunction ANSD Stands for Autonomic Nervous System Dysfunction Risk The correlations between 2h- OGTT Glucose and Cardiometabolic SudoD Risk score (CMRS) were: r = 0.56 (p = 0.003). Stands for Sudomotor Dysfunction Risk Small fiber neuropathy risk using the sudomotor response score had Stands for Endothelial Dysfunction Risk a sensitivity of 91.4 % and specificity of 79.1% to detect diabetic neuropathy symptoms score >=1. Stands for Insulin Resistance CMR PTG CVD is calculated from the PTG spectral analysis markers. Stands for Cardiometabolic Risk Comparing group with CAD and control group, spectral Analysis Markers have a sensitivity of 84.6% and specificity of 96.8% to Stands for Small Fiber Neuropathy Risk detect CAD. Off label use. Results have been tested in clinical studies. Stands for Cardiac Autonomic Neuropathy Risk PTG CVD PTG CVD Stands for PTG Cardiovascular Disease Risk Status Report Show Compared Visits Borderline

## **Insulin Resistance (IR)**

Correlates to the fourth Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

There are no symptoms that can tell a patient Insulin Resistance is present by the way he/she feels. Likewise, a patient won't know if he/she has most of the other conditions that are a part of Insulin Resistance Syndrome (high blood pressure, low "good" cholesterol levels and high triglycerides). That said, the following symptoms could potentially be flags to check further for Insulin Resistance:

- Blurred Vision
- Elevated Blood Sugar
- Extreme Thirst
- Fatigue
- Increased Hunger

Ultimately, patient must see a doctor for an evaluation to determine if IR is a possible diagnosis.

#### **Possible Condition(s)**

Insulin Resistance

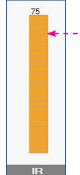
#### **Additional Testing**

(At physician's discretion)

- A1C
- Blood Glucose Testing

#### **Supplemental Data**

Refers to the graph shown on the page above. Physician evaluation recommended if the following marker is elevated (yellow) or abnormal (orange):



- IR is a marker for Insulin Resistance. High numbers indicate an increased risk of heart and metabolic disease and the need for weight management through optimization/diet modification.

#### **Overview:**

Insulin resistance (IR) is the diminished ability of cells to respond to the action of insulin in transporting glucose from the bloodstream into muscle and other tissues. IR typically develops with obesity and heralds the onset of type 2 diabetes.

It is as if insulin is "knocking" on the door of the muscle. The muscle hears the knock, opens up, and lets glucose in. But with IR, the muscle cannot hear the knocking of the insulin ("resistant"). The pancreas makes more insulin, which increases insulin levels in the blood and causes a louder "knock."

Eventually, the pancreas produces far more insulin than normal and the muscles continue to be resistant to the knock. As long as one can produce enough insulin to overcome this resistance, blood glucose levels remain normal. Once the pancreas is no longer able to keep up, blood glucose starts to rise, initially after meals, eventually even in the fasting state. Type 2 diabetes is now overt.

IR is defined clinically as the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population. Insulin action is the consequence of insulin binding to its plasma membrane receptor and is transmitted through the cell by a series of protein-protein interactions.

Two major cascades of protein-protein interactions mediate intracellular insulin action: one pathway is involved in regulating intermediary metabolism and the other plays a role in controlling growth processes and mitoses. The regulation of these two distinct pathways can be dissociated.

Several mechanisms have been proposed as possible causes underlying the development of insulin resistance and the insulin resistance syndrome. These include: (1) genetic abnormalities of one or more proteins of the insulin action cascade; (2) fetal malnutrition; and (3) increases in visceral adiposity. IR occurs as part of a cluster of cardiovascular-metabolic abnormalities commonly referred to as "The Insulin Resistance Syndrome" or "The Metabolic Syndrome".

This cluster of abnormalities may lead to the development of type 2 diabetes, accelerated atherosclerosis, hypertension or polycystic ovarian syndrome depending on the genetic background of the individual developing the insulin resistance.

## Cardiometabolic Risk (CMR)

Page 3 of a sample Physician's Full Report Summary.

Patient Name: Test Patient Page 3 Weight: 209 Lbs BMI: 33.7 STATUS REPORT 5' 6" Height: PHYSICIAN'S FULL REPORT SUMMARY Date of birth: 9/7/1973 Gender: Male ▼ Disease Lab Tests Symptoms Treatment Cardiometabolic Risk Overview **Risk Factors Chart Meaning:** ANS1 Cardiometabolic Risk Score Markers PTG CVD Risk Score Systolic = Systolic pressure Diastolic = Diastolic Systolic ANS1 CMR pressure >= 40 Vs PTGVLFi RI = Marker of medium artery stiffness PTGTP T. Power PTGVLFi = Homeostatic Marker\* PTGTP = Stress.I PTG R Homeostatic Marker\* STRESS.I = Marker of hepatic glycolysis FM = Fat mass T. Power = Marker of ANS overall activity PTG CVD ESRNO = Marker of skin microcirculation PTG I = Homeostatic Marker\* PTG R = Homeostatic Marker\* CAN S. = Cardiac Autonomic Neuropathy Score CMR = Cardiometabolis Risk CVD = Cardiovascular Disease PTCVLF Cardiometabolic Risk Scores PTG CVD Risk Score Item Score Items . Item Score Items Item Score <u>Items</u> Color Code Items Item Score \* Homeostatic Marker are correlated to LF/HF BMI Abnormal 2 PTG I Systolic 0 0 autonomic nervous system and endothelial Borderline T.Power Diastolic PTGTP 2 1 **PTGVLF**i 0 Normal Range Stress.I **ESRNO** 2 PTG R function ANS Overview Dashboard PTG Analysis Visits Listed Compare Last 3 11/18/2014 19:40 > Off label use. Results have been tested in clinical studies.

## Cardiometabolic Risk (CMR)

Correlates to the fifth Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

- Dizziness
- Headaches
- Myocardial Infarction
- Ankle Swelling

#### **Possible Condition(s)**

- High Cholesterol
- Heart Disease
- High Blood Pressure
- Diabetes

#### **Additional Testing**

(At physician's discretion)

- Cholesterol
- Blood Pressure Checks
- Hemoglobin A1C
- Glucose Testing (BG, OGTT, Etc)
- Ankle Brachial Index (ABI)
- CBC (Complete Blood Count)
- Carotid Ultrasound
- CMP (Complete Metabolic Profile)

#### **Supplemental Data**

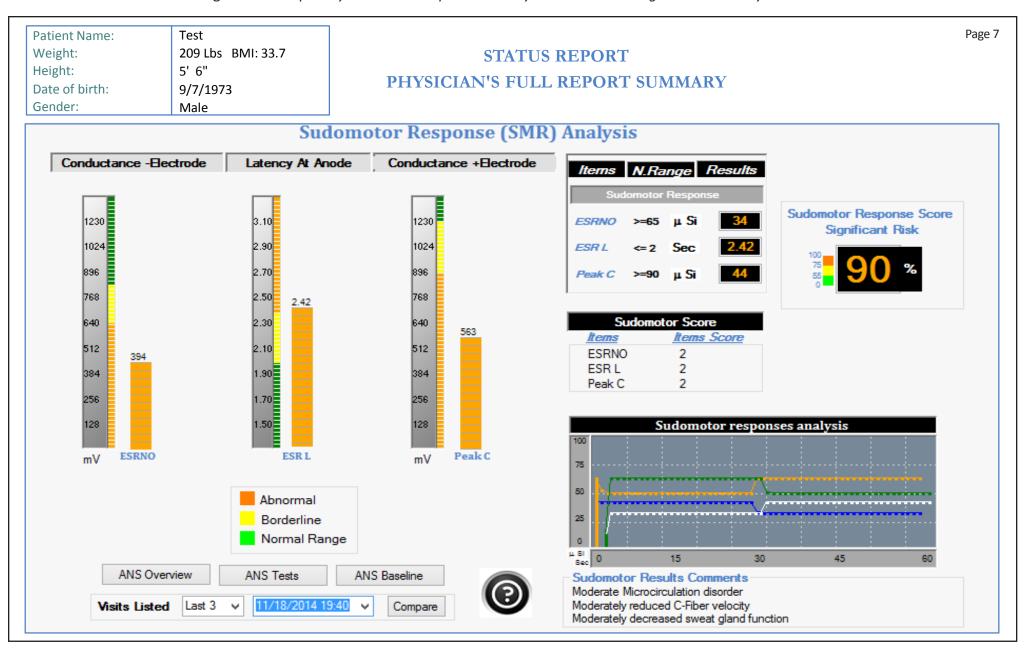
Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):

- 1 RI is a marker for atherosclerosis, showing small and medium arterial stiffness.
- **2 LF/HF** indicates ANS balance. If the value is high (greater than 2), it indicates sympathetic system predominance and the possibility of mental stress or anxiety. If the value is low (less than 0.5), it indicates parasympathetic system predominance and the possibility of fatigue or depression.
- 3 PTGTP helps identify risk of insulin resistance and therefore pre-diabetes as well as possible heart disease and metabolic disorders. High numbers may be associated with fatty liver and atherosclerosis. May need to modify diet and increase exercise.
- 4 STRESS.I correlates to C-reactive Protein (CRP) and is a marker for sympathetic failure. High numbers indicate a risk for heart disease.
- **5 BMI** measures body fat based on weight in relation to height, and applies to most adults age 20 and over. According to the 2010 Affordable Care Act, if a patient is over a 27 BMI with at least two co-morbidities (or 30 BMI or higher with no

- co-morbidities), a physician must offer obesity counseling (which is Medicare and private insurance reimbursable). If they do not, and are not on Electronic Health Records (EHR), their Medicare reimbursements may be reduced up to 5% starting in 2018 (according to the Meaningful Use Program.)
- **T.Power** is the main indicator of ANS activity. Low numbers may indicate a sedentary lifestyle and may indicate the need to increase activity. TP may also define the variability, or degree of fluctuation, in the length of the intervals between beats. A low HRV score is associated with poor prognosis for patients who are post Myocardial Infarction (MI) and at an increased risk of autonomic neuropathy in the diabetic population.
- **ESRNO** is a marker of electrical skin response to nitric oxide (NO) production and vasodilation. This marker reflects microcirculation blood flow. Decreased ESRNO indicates microcirculation issues. Low numbers indicate signs of poor micro vascularization and an increased risk of distal neuropathy.

## **Small Fiber Sensory Neuropathy (SFN)**

Page 7 of a sample Physician's Full Report Summary reveals SFN through the SMR Analysis below.



## **Small Fiber Sensory Neuropathy (SFN)**

Correlates to the sixth Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

- Burning Sensations
- Painful Contact with Socks or Bed Sheets
- Pebble or Sand-Like Sensation in Shoes
- Pins and Needles Sensation in Feet
- Stabbing or Electrical Shock Sensation

#### **Possible Condition(s)**

• Small Fiber Neuropathy

#### **Additional Testing**

(At physician's discretion)

- Skin Biopsy
- Nerve Conduction Testing
- Other Pain
   Management Testing

#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):



**ESRNO** is a marker of electrical skin response to nitric oxide (NO) production and vasodilation. This marker reflects microcirculation blood flow. Decreased ESR NO indicates microcirculation issues. Low numbers indicate signs of poor micro vascularization and increased risk of distal neuropathy.

**ESR L** is a marker of sweat gland nerve density. This marker reflects post sympathetic nerve density. The peak reflects C-fiber density. Low numbers are an early detection of peripheral distal neuropathy.

**Peak C** is a marker of sweat gland function and reflects maximum number of water and chlorine released on the electrode plate after stimulation. Decreased Peak C is either due to nerve damage or hypohidrosis (low sweat). An abnormal number (high or low) can be attributed to hyperhidrosis. (Excessive Sweat): Low numbers are found with nerve damage.

## **Cardiometabolic Autonomic Neuropathy (CAN)**

Page 5 of a sample Physician's Full Report Summary reveals CAN through ANS Tests Analysis page, below.

Patient Name: Test

Weight: 209 Lbs BMI: 33.7

Height: 5' 6"
Date of birth: 9/7/1973
Gender: Male

## STATUS REPORT PHYSICIAN'S FULL REPORT SUMMARY

Page 5

Autonomic Nervous System (ANS) Tests Analysis RR Intervals Valsalva RR Intervals Standing Items N.Range Results ANS Response Failure Risk Factors Sympathetic Parasympathetic Blood pressure baseline Risk Factors 955 955 Failure Risk Factors Systolic.P <= 140 mmHg 824 824 693 693 Diastolic P <= 90 mmHg 562 562 >= 2.8 L/min/m2 431 431 SVR = <= 1500 dyn-s-cm2 1300 5 10 15 20 25 30 35 40 Symp. response markers RR Intervals Deep Breathing 688 Valsalva Beat to Beat SP Standing blood pressure 160 150 140 130 Systolic.P <= 140 mmHg 890 772 654 536 418 Diastolic P <= 90 mmHg 120 110 Beat To Beat SP Valsalva R. 100 SPRV2 <-20 ->-40 mmHg 10 15 20 25 30 35 40 ma/sec 0 **BP Standing Response** Baseline Standing Up DPRS <=5 and >= -10 mmHg 220 220 SPRV2 DPRS K30/15 SPRS <= 10 and > -10 200 200 mmHg 180 180 ParaSymp, response markers PSymp. Risk Score 160 160 Item Score Item Score 140 140 Valsal va ratio >= 1.18 120 120 SPRS E/IR 2 K30/15 >= 1.10 100 100 2 2 SPRV2 Vals.R 80 80 E/IR >= 1.18 DPRS K3015 60 ANS Overview ANS Baseline Systolic Diastolic Systolic Diastolic Sudomotor Tests Off label use. Results have been tested in clinical studies.

## **Cardiometabolic Autonomic Neuropathy (CAN)**

Correlates to the seventh Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### **Possible Symptoms**

- Blurred Vision
- Cold, Clammy, Pale Skin
- Depression
- Fainting (Syncope)
- Fatigue
- Dizziness or Lightheadedness
- Lack of Concentration
- Nausea
- Rapid, Shallow Breathing
- Thirst

#### Possible Condition(s)

Hypotension

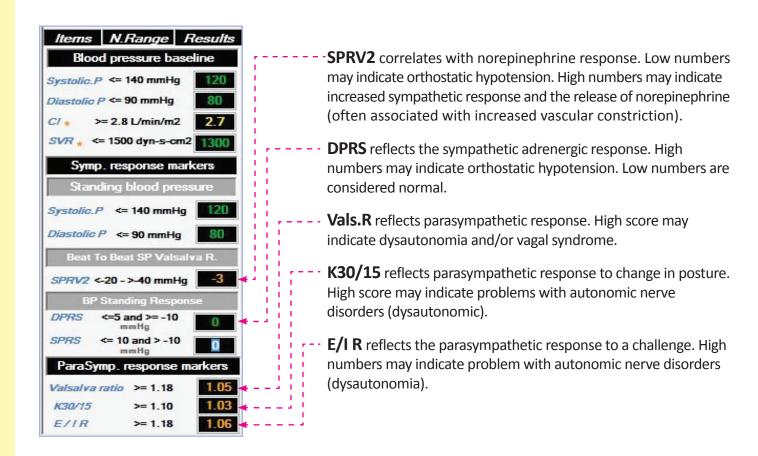
#### **Additional Testing**

(At physician's discretion)

- Blood Glucose
- EKG
- Echocardiogram
- Cardiac Ultrasound
- Holter Monitor
- Additional Cardiac Testing
- Ankle Brachial Index (ABI)

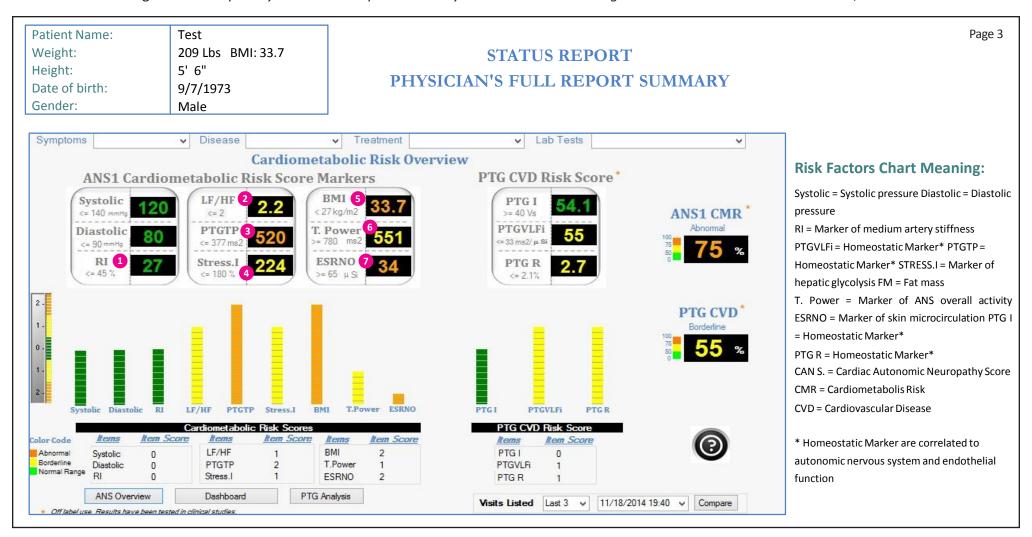
#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):



## Plethysmography Cardiovascular Disease (PTG CVD)

Page 3 of a sample Physician's Full Report Summary reveals PTG CVD through the Cardiometabolic Risk Overview, below.



## Plethysmography Cardiovascular Disease (PTG CVD)

Correlates to the eighth Risk Factor Bar on the graph on Page 1 of Physician's Full Report Summary

#### Possible Symptoms/ Condition(s):

- Aortic Aneurysms
- Atrial Fibrillation
- Cardiomyopathy
- Endocarditis
- Heart Attack
- Stroke
- Venous Thrombosis

#### **Additional Testing**

(At physician's discretion)

- Coronary Artery Testing
- Cardiometabolic
- Ankle Brachial Index (ABI)
- Profile Lab Tests
- BNP (Brain Natriauretic Peptide)
- Carotid Total Plaque Area, LDL-P

#### **Supplemental Data**

Refers to the graphs shown on the page above. Physician evaluation recommended if the following markers are elevated (yellow) or abnormal (orange):

- 1 RI is a marker for atherosclerosis, showing small and medium arterial stiffness.
- **2 LF/HF** indicates ANS balance. If the value is high (greater than 2), it indicates sympathetic system predominance and the possibility of mental stress or anxiety. If the value is low (less than 0.5), it indicates parasympathetic system predominance and the possibility of fatigue or depression.
- **9 PTGTP** helps identify risk of insulin resistance and therefore pre-diabetes as well as possible heart disease and metabolic disorders. High numbers may be associated with fatty liver and atherosclerosis. May need to modify diet and increase exercise.
- **STRESS.I** correlates to C-reactive Protein (CRP) and is a marker for sympathetic failure. High numbers indicate a risk for heart disease.
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- co-morbidities), a physician must offer obesity counseling (which is Medicare and private insurance reimbursable). If they do not, and are not on Electronic Health Records (EHR), their Medicare reimbursements may be reduced up to 5% starting in 2018 (according to the Meaningful Use Program.)
- **T.Power** is the main indicator of ANS activity. Low numbers may indicate a sedentary lifestyle and may indicate the need to increase activity. TP may also define the variability, or degree of fluctuation, in the length of the intervals between beats. A low HRV score is associated with poor prognosis for patients who are post Myocardial Infarction (MI) and at an increased risk of autonomic neuropathy in the diabetic population.
- **ESRNO** is a marker of electrical skin response to nitric oxide (NO) production and vasodilation. This marker reflects microcirculation blood flow. Decreased ESRNO indicates microcirculation issues. Low numbers indicate signs of poor micro vascularization and an increased risk of distal neuropathy.

АВІ	Ankle Brachial Index
AIPTG	A measure of systemic arterial stiffness derived from the ascending aortic pressure waveform. AIPTG is a marker of the LDL cholesterol level. Normal <= 0.45
ANS	The Autonomic Nervous System which is responsible for the control of bodily functions not consciously directed, such as breathing, heartbeat, and digestive processes.
ANS1 CMR	Stands for ANS1 Cardiometabolic Risk Score in percent with a scale of 0 to 100%.
ANSa Score	Stands for Autonomic Nervous System Activity Score and is shown in percent with a scale of 0 to 100%.
ANSb Score	Stands for the Autonomic Nervous System Balance Score at Baseline and is represented in percent with a scale of 0 to 100%.
ANSD	ANS Dysfunction is based on heart rate variability (HRV) analysis at rest and it comprises ANS activity and the balance of sympathetic and parasympathetic systems.
ANSD R	ANS Dysfunction Risk is represented by a scale of 0 to 100%.
ANSR	ANS Risk provides the data for detection of small fiber neuropathy (see below).
ANS CMR	ANS Cardiometabolic Risk is represented by a score in percent with a scale of 0 to 100%.
CAN	Cardiac Autonomic Neuropathy is a risk marker for mortality and cardiovascular morbidity, and possibility a progression promoter of diabetic neuropathy. In addition, CAN increases the risk of hypoglycemia in diabetic patients undergoing treatment.
CAN R	Cardiac Autonomic Neuropathy Risk is assessed from the seven autonomic cardiovascular indices recommended by the Cardiac Autonomic Neuropathy Subcommittee of the Toronto Consensus Panel on Diabetic Neuropathy. It is represented in a percent from 0 to 100%.
Cls	Cardiac Index is an indicator that relates the cardiac output (CO) to body surface area (BSA). Normal >=2.8 L/min/m2
CMR	Cardiometabolic Risk Score is determined by various markers of the exam. At 120 minutes, the co-efficient of correlation between the OGTT and CMR score was r=0.56 (p=0.004) for glucose, r=0.53 (p=0.006) for insulin, and r=0.58 (p=0.002) for C-peptide. Based on a clinical study comparing diabetes patients to healthy controls, CMR score had a sensitivity of 91.7% and specificity of 80% as marker for diabetes.
DPRS	Diastolic Pressure Response to Standing is the difference between the sitting diastolic minus the standing diastolic pressure. Normal <=5 - >=10 mmHg
Diastolic P	Refers to the pressure of the blood in the artery when the heart relaxes. Normal <=90 mmHg
E/IR	Expiration and Inspiration Ratio is calculated by the longest RR Interval divided the shorter RR Interval during the deep breathing test. It reflects parasympathetic systems cardiovagal response to a challenge.
EndoD	Endothelial Dysfunction is the earliest clinically detectable stage of cardiovascular disease EndoD is determined by photoplethysmography analysis.
EndoT Score	Endothelial Dysfunction is the earliest clinically detectable stage of cardiovascular disease. The score is measured in percent from 0 to 100%.
ESR L	Electrical Skin Response Latency is a marker of sweat gland nerve density. This marker reflects post sympathetic nerve density. The peak reflects C-fiber density. Low numbers are an early detection of peripheral distal neuropathy. Normal <=2 Sec
ESR NO	Electrical Skin Response Nitric Oxide is a marker that reflects microcirculation blood flow and increased risk of distal neuropathy. Normal $>=52 \mu \text{ Si}$

HF	High Frequency is an indicator of the parasympathetic system. Normal >=220 ms2
Homeo Score	Homeostasis Score comprises the PTG Spectral Analysis main markers. Studies showed the homeo score had a sensitivity of 84.6% and a specificity of 98% to detect patients with atherosclerosis. It is measured in percent from 0 to 100%.
HR	Heart Rate per minute is calculated from the second derivative of the oximeter wave form. Normal <=90 bpm
IR	Insulin Resistance is a strong risk factor of impaired glucose tolerance (IGT), type 2 diabetes (T2DM) and cardiovascular diseases. Studies show that Metformin treatment or lifestyle changes could reverse it. Comparing our PTG TP marker vs the HE Clamp, our marker has a sensitivity of 90% and specificity of 90% to detect M value < 4.5 (P.0.0001) and therefore insulin resistance.
K30/15	Evaluates the change in heart rate in the standing position. It reflects the parasympathetic system cardiovagal response to the change of posture. It is considered an index of cardiovascular function. Normal >=1.10
LF/HF	Low Frequency/High Frequency is a marker for ANS and mental stress. A value >2 indicates mental stress.
LVETi	Left Ventricle Ejection Time Index is adjusted with the heart rate.
Parasympathetic Nervous System	This is part of the involuntary autonomic nervous system that is responsible for slowing the heart rate, increasing intestinal and glandular activity, and relaxes the sphincter muscles. The parasympathetic along with the sympathetic nervous system make up the ANS.
Peak C	Peak C is a marker of sweat gland function and reflects maximum number of water and chlorine released on the electrode plate after stimulation. Decreased Peak C is either due to nerve damage or hypohidrosis (low sweat). An abnormal number (high or low) can be attributed to hyperhidrosis (excessive sweat). Low numbers are found with nerve damage. Normal >=90 μ Si
PEP	Stands for the Pre-Ejection Period. Studies have shown that PEP is inversely correlated with left ventricle contractibility. Normal <= 110 ms
PEPi/LVETi	Pre-Ejection Period index/Left Ventricle Ejection Time index ratio has been shown in studies to correlate to cardiac performance. Normal = 0.35
pNN50	An indicator of the heart rhythm stability. Normal >=10%
Power HF	An indicator of the parasympathetic or vagal activity in the area of the spectral analysis. Normal >=220 ms2
Power HF nu	An indicator of the parasympathetic or vagal activity expressed as percent of the total power. Normal >=22%
Power LF nu	An indicator of both sympathetic and parasympathetic systems expressed as percent of the total power. Normal <=46%
Power LF	An indicator of both sympathetic and parasympathetic systems expressed in area of the spectral analysis. Normal >=220 ms2
PTF Score	Parasympathetic Test Failure Score is important because parasympathetic failure could increase cardiovascular events; and it is an indicator of CAN. It could also be associated with symptoms of dizziness or orthostatic hypotension. It is measured in percent from 0 to 100%.

PTG CVD	The Photoplethysmography Cardiovascular Disease risk is based on the homeostatic markers issued from the PTG spectral analysis (PTGi, PTGVLFi, and PTGr). Our studies demonstrate that PTGi, PTGVLFi and PTGr are respectfully correlated to endothelial dysfunction, autonomic dysfunction and artery blood flow. Endothelial dysfunction, ANS dysfunction, and artery blood flow are known risk factors for atherosclerosis, and our study showed the PTG CVD score had a sensitivity of 82.5% and specificity of 96.8%, at a cutoff of 2, when used to detect Coronary Artery Disease (CAD). If above is in the yellow or orange range, generally look at performing an Ankle Brachial Index (ABI) or other acceptable device for verification and edification. As always, this decision is based on physician's determination of Medical Necessity.
PTG CVD R	This stands for risk score in percent with a scale of 0 to 100%.
PTGI	The Photoplethysmography Index of the Spectral Analysis Components has been shown in studies to detect endothelial dysfunction and has a specificity of 88% and sensitivity of 86%. At the 120 minute assessment of the OGTT, the correlation between glucose and PTG i r=minus 0.56, p=0.003. Normal >=40 Vs
PTG R	The Photoplethysmography Ratio is calculated from the Spectral Analysis Components (PTGVLF/PTGi). Normal <=21%
PTGLF	Plethysmograph – Very Low Frequency has been shown in studies to be inversely correlated with arterial blood flow. Normal <=100 ms2
PTGVLFi	Photoplethsmography – Very Low Frequency Index is an algorithm calculated from PTGVLF and adjusted with a sudomotor marker (Baseline). Studies show that PTGVLFi has a specificity of 88% and a sensitivity of 92% comparing diabetic patients and control group. Normal <=33 ms2/μ Si
RI	Reflection Index is an indicator of stiffness of the small and medium arteries of the circulatory system and is a marker for atherosclerosis. Normal <=45%
RMSSD	The Root Mean Square of the Successive Differences is an indicator of parasympathetic activity and reflects the electrical stability of the heart. Normal >=35 ms
RR Intervals	The intervals between each heartbeat. Normal >= 670 ms
SD ba	Standard Deviation Baseline is taken from the height of the 2nd point of the 2nd derivative of the original waveform (Acceleration Algorithm). Studies have shown that SD ba has a good correlation with Framingham Risk Score. Normal <=0.95
SD da	Standard Deviation Data is taken from the height of the 4th point of the 2nd derivative of the original wave form (Acceleration Algorithm). Studies have shown that SD da has a good correlation of angiotensin activity. Normal <=0.42
SDNN	Standard Deviation of Normal to Normal intervals is calculated by the square root of the variance. SDNN should be an indicator of both sympathetic and parasympathetic regulation and as a marker of VO2 (measure of the volume of oxygen used by the body) maximum in patients not undergoing any treatment. Normal >=40 ms
SFN	Small Fiber Neuropathy is assessed through the ANSR score. SudoD score is based on decreased results and reflects the reduction of activated sweat gland density. However, a low score of SudoD based on increased results could be a sign of small fiber inflammation in elderly patients and could provide the same symptoms. Based on the clinical study comparing the diabetes subgroups with Diabetic Neuropathy Symptoms (DNS) Score >=1 and the diabetes patients group with DNS Score =0, SMR. Score had a sensitivity of 91.4% and specificity of 79.1% to detect DNS>=1 in diabetic patients (P=0.0001).
SpO2%	Peripheral Capillary Oxygen Saturation shows the percentage of oxygen saturation in the hemoglobin. Normal >95%

SPRS	Systolic Pressure Response to Standing is the difference between the sitting systolic pressure minus the standing systolic pressure. Normal <=10 - >10 mmHg
STA Score	Sympathetic Test Assessment Score assesses the sympathetic response which could increase cardiovascular events. Sympathetic failure is an indicator of CAN. It is measures in percent from 0 to 100%.
SPRV2	Systolic Pressure Response to the Valsalva maneuver in phase 2. SPRV2 is correlated with norepinephrine response. Normal <20 - >40 mmHg
STRESS I (Stress Index)	Stress Index reflects the sympathetic system activation which may increase the hepatic glycolsis and hepatic insulin resistance. Stress I has a sensitivity of 94.5% and specificity of 31.8% comparing diabetic patients and control group. Normal <=180%
SudoD	Sudomotor Dysfunction is defined as decreased sudomotor activity. SudoD is the earliest clinically detectable sign of autonomic neuropathy in populations at high risk, such as diabetic patients.
Sympathetic Nervous System	The part of the ANS that contains chiefly adrenergic fibers and tends to depress secretion, decrease the tone and contractility of smooth muscle(s), and increase heart rate.
Systolic P	This refers to the pressure of the blood in the artery when the heart contracts. Normal <=140 mmHg
T.Power	Total Power is the main indicator of the ANS activity. The TP is also used in peer reviews to define the total Heart Rate Variability (HRV) score. Normal >=780 ms2
Vals. R	Valsalva Ratio identifies subsequent tachycardia / bradycardia during the Valsalva maneuver which are baroreceptor mediated. Normal >=1.18
VO2	A measure of the Volume of Oxygen used by the body.