PD2i Cardiac Analyzer™ – Putting It Into Practice.
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After reading this document you will have an understanding of the clinical utility of the PD2i Cardiac Analyzer™. The patients of interest here are our DM, CAD, HTN, and CHF clients. The Ewing ratios and the PD2i® score produced by the device are simply the latest diagnostic data to be used in a CV assessment. They are measures of autonomic health and have strong mortality and treatment implications.

The PD2i® Score

The PD2i® score has FDA approval for use in patients undergoing cardiovascular disease testing. Published clinical studies demonstrated that a score ≤ 1.4 is suggestive of cardiac autonomic dysfunction and may warrant further evaluation as causes include autonomic dysfunction due to medical condition, ischemic disease or cardiomyopathy. This would be analogous to discovering inverted T-waves in the inferior leads of the ECG of a 60 year old male with HTN. The ECG finding is not diagnostic of CV disease, digoxin effect or electrolyte disturbance but it is certainly not reassuring and warrants further evaluation. Upon discovery of a low PD2i® score in a CV patient, my next steps would usually be a stress test and an echocardiogram

A high PD2i® score can provide some reassurance when evaluating nonspecific chest and abdominal symptoms. There is an ER study (attached, TCRM 2008 ER) that had over 900 non-low risk patients who were evaluated for chest pain who also had PD2i® testing. A score ≤ 1.4 showed a 96% sensitivity and 85% specificity for predicting arrhythmic death within one year as loss of heart rate variability parallels susceptibility to ventricular fibrillation. A score above 1.4 had a 99% *negative* predictive value for arrhythmic death at 1 year. As you know, it is not the infarction that is fatal; it is the subjects' electrical response to the ischemia mediated via the autonomics – to fib or not to fib! **The PD2i® score should not be used to exclude cardiac ischemia.**

Lastly, I use the PD2i® score as leverage with reluctant ICD candidates. Many patients recognize that our current implantation criteria of an EF ≤ 35% is sensitive but lacks specificity, as only one out of 5 recipients ever receive appropriate discharge. The MUSIC trial showed that in persons with CHF and an EF ≤ 35%, a PD2i score of ≤ 1.4 predicted twice the mortality rate (see the attached slide). These persons should move to the front of the defibrillator/resynchronization implantation line as their separation from those with scores above 1.4 is rapid!

Clinical decision making for the CV patient involves the assimilation of the history, the exam and the objective CV data (PD2i Analyzer results, ECG, Echo, Holter, Nuclear ST, CXR, MUGA, etc.). The PD2i score is new, useful measure of CV health that should not be used in isolation, but in context. Cardiologist, Dr. Mitchell Karl has developed a couple of management pathways I think are helpful in incorporating the score into your practice. They are attached.

Looking forward, you can expect to see more of the PD2i® score as it is being studied at the University of Mississippi Medical Center as the "new vital sign" in acute care and at the Wingate Institute in Israel in sports medicine. The PD2i score has been shown to acutely fall with physiologic stress (volume loss, hypoxia, hypotension, acidosis, etc.). Serial (15 min) PD2i scores in trauma, ICU, ER, and OR settings are showing much promise as being the earliest parameter to change (relative to HR, BP, or clinical impression) as a patient decompensates or responds to therapy. This makes sense as the autonomic nervous system is constantly active and attempting to achieve

homeostasis (BP, pH, temp) through various mechanisms. A drop in BP is a late finding and reflects exhaustion in the ability to compensate. This has great opportunity to improve patient outcomes in the hospital and field trauma settings.

The Ewing Ratios. This is the second and billable portion of PD2i Cardiac Analyzer™ results. These are three safe, simple physiologic tests that challenge the autonomic nervous system. The components are 1) paced deep breathing for 1 minute, 2) Valsalva against 40 mmHg for 15 sec and 3) coming from a sitting to a standing position for 2 minutes. During these simple maneuvers, the R-R intervals are constantly measured. Two data points at specific positions in each test graphic are used to generate a ratio for each of the 3 tests. This ratio is compared to age and sex established normals to determine if each test is normal or abnormal. Any abnormal test establishes the diagnosis of "abnormal autonomic function" (ICD 337.9).

HRV measurement using the standardized Ewing maneuvers is the recommended method for screening diabetic patients for autonomic nervous system dysfunction by the American Diabetes Association and the American Academy of Clinical Endocrinologist. The rationale for testing and patient care implications of HRV testing is published in Johns Hopkins "Diabetes Guide" in February of this year (all articles attached). Heart rate variability (HRV) testing annually should be routine part the management diabetes - just like annual eye exams, quarterly HbA1c testing and annual urine testing for microalbuminuria. Approximately 20% of diabetics will have abnormal Ewing testing.

It is quite important for the doctor to recognize and appropriately treat patients with abnormal heart rate variability. Although they are most commonly diabetics, other covered diagnosis for evaluation include CAD, CM, HTN, RI, COPD, Asthma, and HTN.

HERE IS WHY?

1. **Increased risk during operations.** The peri-operative cardiac morbidity and mortality in diabetics with cardiac autonomic neuropathy (CAN) are increased 2-3 times over non-diabetics. Additionally, those patients identified as having autonomic dysfunction can benefit from the anesthesia recognizing that they are more prone to hypothermia and hypotension.
2. **Be especially alert for silent MI in these diabetic patients.** Because of the reduced appreciation of cardiac ischemic pain in persons with CAN, underlying cardiac disease may project minimal symptoms. Silent MI is twice as prevalent in diabetics with CAN. Vague symptoms, such as cough, unexplained nausea, unexplained dyspnea, new fatigue or subtle ECG changes, should prompt the physician to evaluate for ischemia in this diabetic subset with extra caution as they have a 2x increase in mortality. **(In summary, silent MI is twice as common and twice as fatal if a diabetic has CAN.)**
3. **Hypoglycemic Unawareness**. The patient with autonomic impairment may not experience the early symptoms of sweating or rapid heat rate before developing a dangerously low blood glucose that could cause a fatal accident. I make sure the patient and the family understand this potential problem and recommend liberal glucose testing and consider less than "tight control" as our goal.
4. **Orthostatic hypotension.** Persons with CAN should be educated that they are at risk of excessive blood pressure drops upon standing. Symptoms may include dizziness, weakness, and faintness to vision loss or even fainting. One sees this frequently in

longstanding diabetics and octogenarians In addition to education, interventions include mineralocorticoids (florinef), sympathomimetic agents (midodrine, pseudoephedrine, clonidine), caffeine, B-adrenergic blockers (propranolol), DDAVP, pressure graduated stockings, liberal salt and water intake. They should be advised take extra precautions with showers and hot baths, during warm weather, after exercise and with fevers. The prescriber should be cautious with antihypertensives, anti-anginals, antidepressants and diuretics that may worsen the symptoms.

5. **Explain resting tachycadia**. CAN patients may have resting heart rates of 90-100 beats per minute that is often unresponsive to exercise. This needs to be addressed medically (with beta-blockers) in patients with known coronary disease and not confused with hyperthyroidism, anxiety or de-conditioning.
6. **Medication Adjustment.** Ca blockers and particularly, B-Blockers can suppress **sympathic** tone resulting in fatigue, depression and sexual dysfunction that the patient just accepts because they attribute the symptoms to their disease state (DM, CAD, CHF) or their age. If ANS testing as abnormal and the patient is on these meds, I inquire about depression, fatigue and sexual dysfunction. If any of these symptoms are present, I will reduce the med dose 50%. This usually results in an improvement of the symptom and no change in resting rate, arrhythmia or angina. Quality of life is improved!
7. **Guided exercise programs.** Persons with CAN need to use their “perceived” level of exertion to guide their intensity of exercise, not heart rate. Many persons with CAN are unable to reach the target percentage of their age adjusted maximum heart rate. Attempting to do so might induce a cardiac event or syncope. I consider stress testing in these at risk patients before endorsing an exercise plan.
8. **Gastroparesis**. - Symptoms of gastroparesis can include nausea, reflux, emesis, early satiety, weight loss and bloating. Interventions include medications (Reglan, Amitiza) and modification to a low residue diet. Interestingly, autonomic dysfunction in the gut may alternate with diarrhea - where a high fiber diet and anti-cholinergic drugs can be used for persistent symptoms.
9. **Sudomotor Neuropathy**. Nerve damage may impair sweat gland function. This can lead to heat exhaustion or heat stoke in routine outdoor situations such as gardening or social events. Similarly, creams to the feet should be encouraged as excessively dry skin is prone to cracking and infection.
10. **Visual Impairment.** Autonomic dysfunction of the third cranial nerve, which controls pupil diameter, can impair vision, particularly night vision. I advise patients to consider this in their travel planning.
11. **Use an abnormal test a motivator** for exercise, weight loss and better DM management. Progression ANS dysfunction and its symptoms can be delayed with good DM control.

You will Treat, Educate and Motivate your patients
differently using the PD2i Cardiac Analyzer^{TM}