

FAQ's of PD2i in Cardiology Practice

1. What does PD2i measure?
2. Why is this important?
3. What conditions/diseases can it detect?
4. Which patients are appropriate for PD2i testing?
5. How often should testing be performed?
6. What cardiology related diagnosis codes justify the use of the PD2i Analyzer™?

1. What does PD2i measure?

As applied to heart rate variability, PD2i is a measure of the degrees of freedom (cooperativity or independence) of the different elements of the autonomic nervous system (ANS) that control heart rate (sympathetic and parasympathetic). These elements, known as sensory-motor loops (SMLs), each react to specific sensory input, such as blood pH, body temperature, blood pressure, among others. In healthy individuals, these SMLs behave relatively independently, which causes the normal heart rate variability (HRV) seen in an ECG recording: such an HRV signal would be said to show high degrees of freedom. However, with chronic disease (e.g., congestive heart failure) or acute insult (e.g., trauma), the SMLs coordinate their behavior more; this results in the HRV signal showing lower degrees of freedom as the SMLs work more cooperatively, and is reflected in lower PD2i values.

2. Why is this important?

The ANS is exquisitely sensitive to insult or disease, reacting to abnormal conditions often long before the patient is aware of a problem and before there are any overt manifestations (signs and symptoms). In addition, because the ANS is so good at compensating for such abnormalities, the severity of the condition may continue to be masked and otherwise undetectable even far into the disease process. Because PD2i directly assesses the ANS, it can detect the ANS status and alert the physician that there is an underlying disease process or insult that may not otherwise be apparent. For example, blood volume losses of up to 15% ("Class I hemorrhage") are undetectable using standard vital signs or symptoms. Even beyond a 15% loss, the ANS compensates so well that standard vital signs may still appear normal and the patient may continue to be unaware of the problem. The PD2i value, however, already reflects the volume loss at the 8% level. Similarly, in congestive heart failure (CHF), a greater degree of ANS coordination signifies a more severely affected patient. Patients with a minimum $PD2i \leq 1.4$ are at approximately a two-fold risk of total, cardiac, and CHF mortality. In patients with chest pain, a minimum $PD2i \leq 1.4$ was shown to correlate with an elevated risk of sudden death in the following 12 months.

The PD2i score may also be abnormally low in patients with dysfunction of the ANS itself. Patients with autonomic neuropathy are at elevated risk for anesthesia-related complications and can have numerous somatic complaints, including dizziness, syncope, fatigue, GI symptoms, and sexual dysfunction, among others. Perhaps most important,

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those with cardiac autonomic neuropathy (CAN) are at a two-fold risk of adverse cardiac events. Autonomic neuropathy and CAN are most commonly, but not exclusively, seen among diabetic patients. However, many other disease processes are associated with autonomic neuropathy, including CHF, sleep apnea, and major depression, among others. Since these disorders are also associated with elevated adverse cardiac event rates – as are patients in general with a low PD2i – there seems to be a common thread: one which a PD2i assessment appears to be able to detect.

3. What conditions/diseases can it detect?

- Risk of sudden death in patients with chest pain
- Risk of total, cardiac and heart failure mortality in patients with EF \leq 35%
- Autonomic neuropathy
- Early volume depletion/blood loss
- Risk of mortality at 30 days in ICU patients
- Risk of hypotension in pregnant women delivering at term
- Cardiac allograft transplant rejection.

4. Which patients are appropriate for PD2i testing?

- During the evaluation of patients presenting with such complaints as dizziness, syncope, brady- or tachycardia, fatigue, hypotension, hypertension, GI or GU complaints, and sexual dysfunction, being able to rule in or rule out ANS dysfunction can be invaluable as the differential diagnosis is worked through.
- Patients with symptoms possibly consistent with autonomic dysfunction
- Patients with type II diabetes mellitus (2005 ADA recommendations), to look for the onset of autonomic neuropathy
- Patients undergoing a pre-operative cardiac evaluation, especially if they have either signs & symptoms possibly consistent with autonomic neuropathy or a comorbidity associated with autonomic neuropathy (such as diabetes, Parkinson's, etc.)
- Patients with CHF
- Patients with angina or angina-equivalent symptoms

5. How often should testing be performed?

- The ADA recommends annual screening for autonomic neuropathy for diabetic patients
- As a follow up to a patient with autonomic neuropathy, especially if the associated disease (e.g. CHF) has progressed or if there has been a therapeutic intervention

6. What cardiology related diagnosis codes justify the use of the PD2i Analyzer™?

See the attached material.