Nonlinear parameter of heart rate variability can diagnose early cardiac autonomic neuropathy

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Abstract
This is a case of a 63-year-old female presenting with diabetes mellitus, hypertension, hypothyroidism, and postmenopausal osteoporosis with findings showing abnormal AFT with reduced heart rate variability (HRV) and multiple lobed Poincaré plot, pointing to premature atrial contractions.

Keywords
autonomic function test, heart rate variability, hypertension, nonlinear Poincaré plot, premature atrial contractions

1 | INTRODUCTION

Hypertension and diabetes mellitus increase chances of cardiovascular morbidity. Premature atrial contractions (PACs) have been shown to be strong and independent predictors of incident atrial fibrillation and associated complications, like stroke and congestive heart failure. These morbidities are diagnosed only when the patient is already suffering from the symptoms. Consequently, it is of paramount importance to develop new techniques for early diagnosis prior to any deterioration on healthy patients. The cardiovascular system is controlled and influenced, apart from a unique intrinsic system, by the autonomic nervous system. In a study, lagged Poincaré plot analysis revealed significant changes suggestive of decreased parasympathetic modulation in diabetic patients.1 In this case, increased high frequency and SD1 (which usually denote parasympathetic activity) are found, which can be because of premature atrial contractions.

2 | CASE REPORT

This is a case of a 63-year-old female presenting with diabetes mellitus, hypertension, hypothyroidism, and postmenopausal osteoporosis. She was admitted to the Department of Endocrinology, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow on 6/10/19 with complaints of fever, breathlessness, anxiety, bodyache, with generalized weakness, anorexia, and insomnia, which improved with medication. She was discharged on 9/10/19 and advised medication paracetamol, metformin 500 mg + glimepiride 3 mg tablet (one tablet BD), sitaglipatin 50 mg one tablet BD, Inj Insulin Glargine (24 unit at bedtime), levothyroxine (100 µg one tablet OD), amitriptyline (10 mg one tablet HS), citalopram (10 mg one tablet OD), vitamin D3 (60 000 IU twice a week), and telmisartan, pantoprazole + domperidone (one tablet OD).

Investigations and results.
Investigations performed were thyroid profile, showing decreased TSH (0.12 Uiu/mL), CBC was normal except increased ESR (22 mm/1st
hour), serum electrolytes were normal, KFT and LFT were normal, USG whole abdomen revealed mild hepatomegaly, HSCRP −0.78, HBA1c 7%, BMD measured at spine L1-L4 was very low with a T score of −2.8.

On 13/11/2019, AFT was done as the patient complained of persistent weakness. Results are shown in Table 1 and Figures 1 and 2.

3 | DISCUSSION

Autonomic function tests revealed abnormal standing test and Valsalva ratio and diastolic BP change to sustained handgrip. However, deep breathing test was normal. Thus, there is definite autonomic nervous system (ANS) involvement according to Ewing’s criteria\(^2\) as two of three AFT among parasympathetic tests are abnormal and sympathetic test is abnormal.

A nonlinear method of HRV analysis is Poincaré plot. Poincaré plot in this patient revealed multiple side lobed pattern. Recently, Poincaré plots of arrhythmic ECG data were systematically investigated to discover 10 distinctive prototypical patterns representing different kinds of arrhythmias from 24 hour Holter ECG data. Multiple side lobe patterns specify the presence of atrial premature beats (confirmed in this case by ECG done for HRV (Figure 2). ECG (for very short time) during admission time was normal) or ventricular premature beats. Premature atrial contraction was not excluded in the patient before linear HRV assessment as there was no clue. Such a graph can also be caused if filter is not applied when artifacts give such a multiple side lobe pattern graph. In this case, notch filter and appropriate HF and LF filters were applied. Ectopics can be another cause because of caffeine and alcohol intake which were avoided in this patient before HRV for 2 hours.

HRV revealed increased average rate; normal SDNN and RMSSD (5 minutes); decreased LF/HF ratio and increased HF power; reduced total power. Decreased LF/HF ratio supports the two abnormal parasympathetic tests and abnormal sympathetic test. There is decreased HRV as shown by reduced total power, which increases chances of cardiovascular morbidity.

| Parameters                              | Value                      |
|-----------------------------------------|----------------------------|
| EI Ratio                                | 0.5447:0.3478 = 1.57 (≥1.21 is normal parasympathetic response\(^a\)) |
| Max and min heart rate difference during deep breathing | 172.5-110.1 = 62.4 (≥15 bpm is normal parasympathetic response\(^a\)) |
| 30:15 beat ratio                        | 0.4595:0.4743 = 0.97 (<1.00 is abnormal response\(^a\)) |
| Valsalva ratio                          | 0.4845:0.4380 = 1.1 (≥1.2 is abnormal\(^a\)) |
| DBP changes to sustained handgrip       | 82-84 = 2 mm Hg (≥10 mm Hg DBP change is abnormal\(^a\)) |
| Average RR                              | 509.9 ms                   |
| Median RR                               | 509 ms                     |
| SDRR                                    | 55.2 ms                    |
| Average rate                            | 119 bpm                    |
| RMSSD                                   | 89.98 ms                   |
| Prr50                                   | 21.27%                     |
| Total power                             | 924.9 ms\(^2\)            |
| VLF power                               | 52.54 ms\(^2\)            |
| LF power                                | 58.25 ms\(^2\)            |
| HF power                                | 611.7 ms\(^2\)            |
| LF/HF                                   | 0.09524                    |
| SD1                                     | 63.68 ms                   |
| SD2                                     | 45.16 ms                   |

\(^a\)Ewing’s battery for autonomic function tests.\(^2\)

![Figure 1](image-url) Poincaré plot revealed multiple lobed pattern, found in premature atrial contractions (confirmed by ECG). SD1: 63.68 ms; SD2: 45.16 ms (SD1, standard deviation of Poincaré plot perpendicular to the line of identity; SD2, standard deviation of Poincaré plot along the line of identity; ms, millisecond)
In spite of increased resting average HR, increased HF power (which usually shows parasympathetic activity) is found. This can be explained as HF power and respiratory sinus arrhythmia do not represent vagal tone. However, usually, decreased HF is seen in diabetes and hypertension. It can be said that SD1 is high in this case because of multiple side lobes in the Poincaré plot caused by premature atrial contractions. It is known that SD2/SD1 is an analogy of LF/HF ratio. It is because of high SD1 (which is not a real descriptor in case of nonlinear Poincaré plot) that HF is high. It is said that descriptors like SD1, SD2, SDRR, and SDSD rely on fitting of an ellipse to the plot, thus adequate only for a typical elongated torpedo pattern. It can also be stated that HF can be high not only because of parasympathetic activity but also because of intrinsic abnormality of heart like premature atrial contractions, as in this case. So, other parameters like size, shape, intensity, and texture features should be taken into account in nonlinear Poincaré plot instead of the conventional descriptors, which may mislead the report. Thus, accurate classification of Poincaré plot should be done to detect arrhythmias. The texture features of Poincaré plot may provide more insights into understanding the dynamics of heart rhythm during, for example, from normal sinus rhythm to arrhythmic events.

4 | CONCLUSION

Poincaré plot can be said to be an alternate to ECG as an easy visual representation to diagnose premature atrial contractions. HRV parameters like SD1, SD2, and SDNN are not real predictors of HRV in case of nonlinear Poincaré plot. Poincaré plot may be analyzed before reading other HRV parameters to rule out nonlinear Poincaré plots in which HRV parameters may not reflect only ANS activity but also arrhythmic events. This case emphasizes that HRV can be a useful screening tool for cardiovascular morbidity in hypertensive patients.

ACKNOWLEDGMENT
Dr Shweta Gupta, Dept of Physiology, Dr RMLIMS, Lucknow.

CONFLICT OF INTEREST
The authors declare no conflict of interests for this article.

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How to cite this article: Dubey P, Verma M, John NA, Gutch M. Nonlinear parameter of heart rate variability can diagnose early cardiac autonomic neuropathy. J Arrhythmia. 2020;36:534–536. https://doi.org/10.1002/joa3.12328