

Research Article

Impaired heart response to deep breathing in diabetic cardiac autonomic neuropathy: Importance of age- related normal range

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Abstract

Introduction: Ewing's battery of cardiac autonomic function tests provides a single value ignoring the decline in autonomic function with ageing.

Objective: To derive age related normal range of heart rate response to deep breathing at six respiratory cycles per minute (HRV) from healthy subjects and estimate the prevalence of cardiac autonomic dysfunction in diabetes.

Materials and Methods: HRV was measured in 207 subjects with type 2 diabetes mellitus and 141 healthy subjects matched for age and sex of diabetics. Abnormal scores had been defined as those more than 2 standard deviation below the mean value in controls.

Results: Diabetics had lower HRV compared to controls in above the ≤ 40 year's age groups ($p < 0.0001$). Abnormal HRV expressed in beats per minute for different class intervals of age was: ≥ 40 years: < 17 ; 41-50 years: < 13 ; 51-60 years: < 11 ; ≥ 61 years: < 7 . Abnormal HRV was observed in 11.59% of diabetics.

Conclusion: Single value generates falls negative results among younger and falls positive results among older age groups. Thus age related normal range of HRV is appreciated in defining cardiac parasympathetic dysfunction in diabetics.

Keywords: ageing, normal range of HRV, parasympathetic dysfunction

1. Introduction

Diabetic autonomic neuropathy is associated with unexplained sudden death.^{1,2} Therefore it is crucial to identify diabetics with cardiac autonomic dysfunction for better treatment strategies. Among the bedside cardiac autonomic function tests, heart rate response to deep breathing (HRV) is the most sensitive test for cardiac parasympathetic function.³ According to Ewing's battery of cardiac autonomic function tests HRV less than 10 beats per minute is considered as abnormal irrespective of the age of the subjects.⁴ But HRV is known to decline with ageing.⁵⁻⁷ Therefore it would be appropriate to implement age related normal range in defining cardiac autonomic dysfunction. Thus this study aimed to derive normal range of HRV in different class intervals of age from non-diabetic healthy subjects and define and estimate the prevalence of impaired HRV in type 2 diabetics in different class intervals of age.

2. Materials and methods

This study was done in the outpatient department of medicine of Kasturba Medical College Hospital, Mangalore, India. This study was undertaken after the approval by the institutional ethical committee in accordance with the ethical standards laid down in the Declaration of Helsinki, and obtaining consent from the study participants. This study involved 207 type 2 diabetics aged between 35-79 years of either sex and 141 age and sex matched healthy subjects.

2.1 Study protocol

Cardiac autonomic function was assessed by deep breathing test. The test procedure was done in the morning after the subjects were completely relaxed. The reproducibility of HRV was investigated in 20 study and 20 control subjects by measuring HRV three times on different occasions over a period of 5-7 days and consistent result was confirmed.

2.2 Procedure followed in recording heart rate response to deep breathing (HRV)

HRV was recorded with the subject in supine position, connected to the limb leads of a standard electrocardiogram. Before beginning the test, subjects were taught to breathe at six breaths a minute: five seconds for each inhalation and five seconds for each exhalation. The examiner raised his hand to signal the start of each inhalation and lowered it to signal the start of each exhalation; this was supported by verbal signals. Lead II electrocardiogram was then recorded continuously at a speed of 25 mm/s for 60 seconds while the subject breathed as instructed. The R-R intervals were measured accurately. The change in heart rate was calculated as the difference between the shortest and the longest R-R interval. HRV was expressed as beats per minute.⁸ Abnormal scores had been defined as those more than 2 standard deviation (SD) below the mean value in normal subjects. Scores between 1.5 and 2 SD below the mean value have been called borderline.⁹

2.3 Statistical analysis

Mean and standard deviation of HRV was estimated for different class intervals of age. Frequency of diabetics with impaired HRV is expressed in %. Unpaired t test was used to compare mean values between control study groups.

3. Result

A total of 207 type 2 diabetics and 141 healthy subjects matched for age and sex of diabetics were studied. The mean age of the diabetics was 55.54 ± 10.34 and of control subjects was 55.21 ± 9.59 . The distribution of subjects in different class intervals of age along with

HRV values of control and study group is presented in table 1. Heart rate response to deep breathing was significantly lower in all the class intervals of age except in below or equal to 40 years of age (table 1).

Table 1 Comparison of heart rate response to deep breathing in controls and stud subjects in different class intervals of age. Values are mean \pm SD. Sample size in parentheses

Class interval of age	Controls	Study subjects
≤ 40 years	33.20 \pm 8.05 (n=9)	29.84 \pm 9.16 (n=14) ^{NS}
41-50 years	30.55 \pm 8.49 (n=54)	22.92 \pm 9.13 (n=56) ^{***}
51-60 years	27.19 \pm 7.65 (n=43)	19.49 \pm 7.05 (n=71) ^{***}
≥ 61 years	25.48 \pm 9.19 (n=35)	16.11 \pm 6.66 (n=66) ^{***}

*** p<0.0001 compared to control; NS = non significant compared to control

The estimated prevalence of type 2 diabetics in different class intervals of age along with data on HRV derived from healthy subjects is presented in table 2.

Out of 207 type 2 diabetics studied 53 had cardiac autonomic dysfunction as evidenced by impaired HRV. Out of 53, 11.59% had abnormal and the rest were of borderline. Prevalence of cardiac autonomic dysfunction was higher in diabetic subjects aged between 51-60 years (table 2).

Table 2 Impaired heart rate response to deep breathing and its prevalence in different class intervals of age in type 2 diabetics compared to healthy subjects

Class interval	Normal value (Beats/min)	Abnormal value (Beats/min)	Borderline (Beats/min)	Abnormal response (%)	Abnormal & borderline (%)
≤ 40 years	> 21	< 17	17- 21	7.14%	14.28%
41-50 years	> 17	< 13	13-17	14.28	26.78
51- 60 years	>15	< 11	11-15	11.26	29.57
≥ 61 years	>11	< 7	7-11	9.09	22.72

4. Discussion

The effect of ageing on HRV is well known. All the studies involving to date have found progressive reduction in the response with increasing age.⁵⁻⁷ Our data based on 141 control subjects and 207 patients with type 2 diabetes mellitus were similar (table 1). The tests of the Ewing battery, which were developed with their normal ranges before this was appreciated, contained only one normal range, regardless of age.⁴ Thus, they stand to generate false negative results among younger patients and false positive results among the older age group. Accordingly we observed 53 out of 207 type 2 diabetics with impaired HRV; but only 15 diabetic patients had a HRV less than 10 beats/minute.

The age related normal HRV values derived from the non-diabetic healthy controls for defining cardiac autonomic dysfunction in type 2 diabetics in the present study was higher compared to the findings of previous researchers. In their study normal for different class interval was: 10-40 years: > 18 beats/minute; 41-50 years: >16 beats/minute; 51-60 years: > 12 beats/minute; and 61-70 years: > 8 beats/minute.¹⁰ This discrepancy was probably due to the technique employed in the estimation of HRV. The maximum and minimum heart rate range during six respiratory cycles was employed in the present study whereas in the study of these researchers average of the five maximum and minimum heart rate changes were considered. Secondly we had used age and sex matched control unlike those researchers matched only for age. Nevertheless the normal value stated for different class intervals of age by those researchers is close to the upper range of borderline observed in our study. Our observation along with other researchers' findings emphasizes that age related normal values are very relevant in diagnosis of autonomic dysfunction in patients with diabetes mellitus.

In our study prevalence of parasympathetic dysfunction was observed in 11.59% and borderline in 26.57% of diabetics. In the study of O'Brien *et al* HRV were found to be below 5th percentile control values in 13-26% in type 1 diabetics.¹¹ In the study of Dyeberg *et al* the prevalence of diabetic autonomic neuropathy in the whole diabetic population indicated by abnormal HRV was 27%.¹² In the present study, the prevalence of cardiac autonomic dysfunction rose steadily from 7.14% to 11.26% from 35 years of age to 50 years. Thereafter it declined to 9.09% in diabetics above 60 years. In the study of O'Brien *et al* in type 1 diabetics, the frequency of abnormal autonomic function was greatest in diabetics aged 40-59 years.¹¹ Thus decline in the prevalence of cardiac autonomic dysfunction after the age of 50 years could be due to the very low values of the normal ranges for older people.

However, based on our study it could be concluded that age related normal range of HRV may be more appropriate in defining cardiac parasympathetic dysfunction in type 2 diabetics.

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