

## Evaluation of Parasympathetic Nerve Function Status in Healthy Elderly Subjects

Islam T<sup>1</sup>, Begum N<sup>2</sup>, Begum S<sup>3</sup>, Ferdousi S<sup>4</sup>, Ali T<sup>5</sup>

**Background:** Autonomic control on cardiovascular activity is modified with age. Impaired autonomic nerve functions are common features of patients suffering from cardiovascular diseases particularly in old age. **Objective:** To observe the influence of aging process on parasympathetic nerve function. **Study design:** This observational study was conducted in the Department of Physiology, BSMMU, Dhaka during the period of July 2005 to June 2006. For this purpose, 60 apparently healthy elderly subjects of both sexes were selected as study group and divided into two groups-one group consisted of 30 elderly subjects with age ranged from 51-60 years and another group consisted of 30 elderly subjects with age ranged from 61-70 years. Thirty sex and BMI matched healthy adults with age ranged from 21-30 years were studied as control. **Methods:** Parasympathetic nerve function status of all the subjects were assessed by three simple non-invasive cardiovascular reflex tests. These were heart rate response to valsalva maneuver, heart rate response to deep breathing and heart rate response to standing (30<sup>th</sup>:15<sup>th</sup>). For statistical analysis one way ANOVA (Post Hoc Test) and the Pearson's correlation co-efficient tests were done. **Results:** Mean ( $\pm$  SD) of valsalva ratio were  $1.50\pm 0.23$ ,  $1.32\pm 0.14$  and  $1.28\pm 0.15$ ; HR response to deep breathing test were  $25.36\pm 3.90$ ,  $18.82\pm 3.35$  and  $15.96\pm 3.54$  beats/min; 30<sup>th</sup>:15<sup>th</sup> ratio in standing test were 1.100.06,  $1.05\pm 0.03$  and  $1.04\pm 0.02$  in 21-30, 51-60 and 61-70 years age groups respectively. All the 3 parameters were significantly lower in both elderly groups compared to that of control adults ( $p < 0.001$ ) Again, HR response to deep breathing was significantly lower in 61-70 years age group compared to that of 51-60 years age group. Valsalva ratio and 30<sup>th</sup>:15<sup>th</sup> ratio were also lower in 61-70 years age group than that of 51-60 years group but the differences were not statistically significant. All the 3 parameters were negatively correlated with age which were statistically significant. **Conclusion:** From this study it may concluded that aging process substantially impaired cardiovascular parasympathetic nerve functions.

**Key words:** Cardiovascular reflex test, elderly person.

J Bangladesh Soc Physiol. 2008 Dec;(3):23-28.

For author affiliations, see end of text.

<http://www.banglajol.info/index.php/JBSP>

### Introduction

Aging is a physiological process<sup>1</sup>. With the advancement of age, there is a progressive declination of almost all body functions, including autonomic nerve function<sup>2</sup>. Autonomic nervous system is vital for homeostasis and its potency is gradually reduced with aging. Therefore, the cardiac autonomic

innervations may also be affected with increasing age<sup>3-6</sup>. Thus aging may affect cardiac autonomic nerve functions, mostly heart rate (HR) and blood pressure (BP) regulations which ultimately may lead to the development of many cardiovascular diseases<sup>6</sup>.

Autonomic nervous activity helps in regulation of blood pressure (BP), heart rate (HR), fluid and electrolyte balance<sup>7</sup>. In old age though both sympathetic and parasympathetic systems are affected but parasympathetic involvement appears to be more frequent than sympathetic<sup>8</sup>. As age advances, the parasympathetic tone and baroreflex sensitivity are gradually reduced<sup>9</sup>.

Cardiac parasympathetic nerve function can be assessed by heart rate response to valsalva maneuver (Valsalva ratio)<sup>10</sup>. In Valsalva maneuver, the subject performs sustained forced expiratory effort against an obstructed airway. It has been observed that throughout the straining, release and recovery segment of the maneuver, the H.R exhibits well-defined changes in normal healthy subjects<sup>10</sup>. But in patients with parasympathetic nerve dysfunction, this HR response to Valsalva maneuver is reduced<sup>11-13</sup>. Aging process may also reduce this response<sup>12</sup>. Normally, lower limit of Valsalva ratio is 1.21<sup>12</sup> which may start to fall after the age of 53 years<sup>14</sup>. Again some investigators reported that Valsalva ratio was declined by 0.009 per years of age<sup>15</sup>.

HR response to deep breathing has been proved to be more sensitive diagnostic index for autonomic nerve dysfunction<sup>16</sup>. Normally, during deep breathing HR is increased by equal or more than 15 beats per minute<sup>17</sup>. An increase in resting heart rate and loss of HR variation to deep breathing are the primary indicators of parasympathetic nerve dysfunction<sup>14</sup>. HR variation to deep breathing is decreased progressively with the increasing age<sup>18</sup>.

Again HR response to standing up is also a simple test for assessment of parasympathetic autonomic nerve function. Changing from lying to standing produces an integrated reflex response of the cardiovascular system, which includes alteration in HR<sup>17</sup>. Normally, HR response to standing represented by 30<sup>th</sup>:15<sup>th</sup> ratio is equal or more than 1.04<sup>19</sup>. But this ratio is relatively lower in healthy elderly person<sup>20-21</sup>.

About 15 percent of the current world population exceeds 60 years<sup>9</sup>. Majority of them may have parasympathetic nerve impairment which may be the underlying cause of many diseases especially cardiovascular diseases. Unfortunately most of them remained unnoticed and usually treated without knowing the underlying etiology. With the above background, study of the effect of age on cardiovascular parasympathetic function is important. Though a number of investigations have been undertaken in different countries, no such data is published in our country. Therefore the present study was conducted to observe the parasympathetic nerve function status in healthy elderly person in our population, in order to evaluate the presence of any impairment of the parasympathetic activity in this age.

### Methods

This study was conducted on healthy elderly person to observe the influence of age on cardiovascular parasympathetic nerve activity. It was done in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, from July 2005 to June 2006.

For this, total 90 apparently healthy subjects of both sexes were selected from a slum area of Malibag Wireless gate and BSMMU staff quarter, Paribag, Dhaka and all of them belonged to lower socioeconomic status. Thirty apparently healthy adults with age ranged from 21-30 years were taken as control (group-A and 60 elderly healthy subjects were selected as study group. They were again subdivided into group B which consisted of 30 elderly subjects with age ranged from 51-60 years and group C which consisted of 30 subjects with age ranged from 61-70 years.

The subjects having the history of chronic renal failure, diabetes mellitus, hypertension, heart diseases, cardiac failure and neurological disorder were excluded. Before inclusion into the study all ethical considerations for the subjects were taken in account. An informed written consent was obtained from each subject. A detail

medical, family, personal and socio-economic history was recorded in a prefixed questionnaire. A thorough clinical examination was done. Height and weight of the subjects were recorded and BMI was calculated. The random blood sugar and serum creatinine levels were estimated for exclusion. Subjects were asked to attend the laboratory of Department of Physiology as per schedule and their cardiovascular parasympathetic nerve functions were assessed by heart rate response to valsalva maneuver, Heart rate response to deep breathing and Heart rate response to standing (30<sup>th</sup>:15<sup>th</sup> ratio)<sup>10</sup>.

Data were expressed as mean  $\pm$  SD (Standard deviation). For statistical analysis one way ANOVA (post Hoc test) and Pearson's co-relation co-efficient test were used as applicable. Analysis was done by SPSS program version-12.

### Results

The mean ( $\pm$ SD) of age, height, weight and BMI of the different groups are shown in table I.

Except age all the groups were matched for height, weight and BMI.

Results of parasympathetic nerve function parameters of all groups are shown in table-II. The values of valsalva ratio, HR response to deep breathing and 30<sup>th</sup>:15<sup>th</sup> ratio were significantly lower in both elderly groups compared to those of control. Again the differences in all the parameters between 51-60 years and 61-70 years age groups were not statistically significant except heart rate response to deep breathing.

Result of relationships of parasympathetic nerve function parameters with age are shown in figure-1,2,3. Valsalva ratio, HR response to deep breathing and 30<sup>th</sup>:15<sup>th</sup> ratio were negatively correlated with age. These relationships of age were statistically significant for valsalva ratio ( $r = -0.494$ ,  $p < 0.001$ ), HR response to deep breathing ( $r = -0.745$ ,  $p < 0.001$ ) 30<sup>th</sup> : 15<sup>th</sup> ( $r = -0.568$ ,  $p < 0.001$ ).

**Table-I**

*Mean  $\pm$ SD of age, height, weight and BMI in different groups (n=90)*

Groups	n	Age(Years)	Height(cm)	Weight(kg)	BMI(kg/m <sup>2</sup> )
A	30	26 $\pm$ 2.67 (21-30)	161 $\pm$ 7.93 (150-172)	52 $\pm$ 5.28 (44-64)	20.22 $\pm$ 1.83 (17.36 -23.61)
B	30	56 $\pm$ 2.68 (51-60)	159 $\pm$ 7.33 (148-171)	52 $\pm$ 5.31 (40-60)	20.77 $\pm$ 2.12 (16.49-24.78)
C	30	66 $\pm$ 2.97 (61-70)	158 $\pm$ 7.11 (148-170)	52 $\pm$ 5.82 (40-64)	20.81 $\pm$ 1.96 (16.53-24.89)

#### Statistical analysis

Groups	p values				
A vs B	0.000***	0.310 <sup>ns</sup>	0.944 <sup>ns</sup>	0.278 <sup>ns</sup>	
A vs C	0.000***	0.090 <sup>ns</sup>	0.672 <sup>ns</sup>	0.258 <sup>ns</sup>	
B vs C	0.000***	0.491 <sup>ns</sup>	0.622 <sup>ns</sup>	0.948 <sup>ns</sup>	

Group A: 21-30 years of adults (Control)

Group B: 51-60 years of elderly subjects

Group C: 61-70 years of elderly subjects

Figures in parentheses indicate ranges

\*\*\* = Significant at  $p < 0.001$

ns = Not Significant

n = Number of subjects

**Table-II**  
*Mean±SD parasympathetic nerve function parameters in different groups (n=90)*

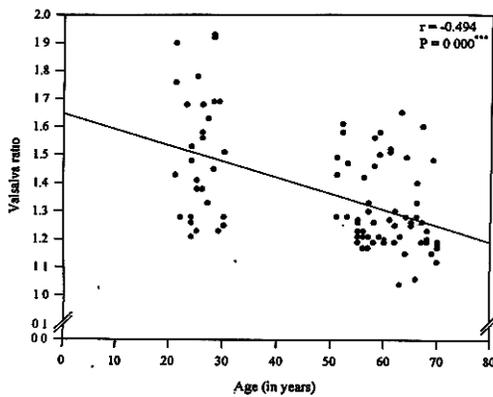
Groups	n	Heart rate response		
		To Valsalva maneuver (Valsalva ratio)	To deep breathing (rate/min)	To standing (30 <sup>th</sup> :15 <sup>th</sup> )
A	30	1.50 ± 0.23 (1.21-1.93)	25.36 ± 3.90 (20.00-32.03)	1.10± 0.06 (1.04-1.28)
B	30	1.32 ± 0.14 (1.17-1.61)	18.82 ± 3.35 (11.67-30.06)	1.05± 0.03 (1.00-1.10)
C	30	1.28 ± 0.15 (1.04-1.65)	15.96 ± 3.54 (9.21-21.28)	1.04± 0.02 (1.00-1.08)

Statistical analysis			
Groups	p values		
A vs B	0.000***	0.000***	0.000***
A vs C	0.000***	0.000***	0.000***
B vs C	0.349 <sup>ns</sup>	0.003**	0.300 <sup>ns</sup>

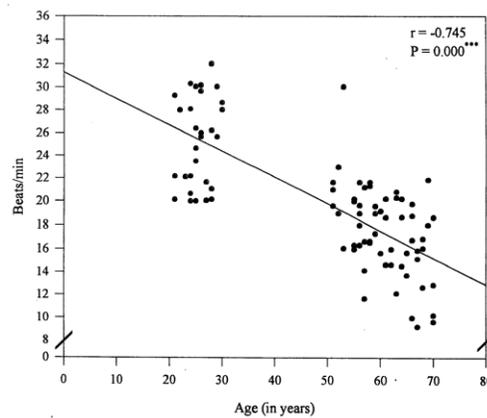
Group A: 21-30 years of adults (Control)  
 Group B: 51-60 years of elderly subjects (study)  
 Group C: 61-70 years of elderly subjects (study)

Figures in parentheses indicate ranges  
 \*\*\* = Significant at p< 0.001  
 \*\* = Significant at p< 0.01  
 ns = Not Significant  
 n = Number of subjects



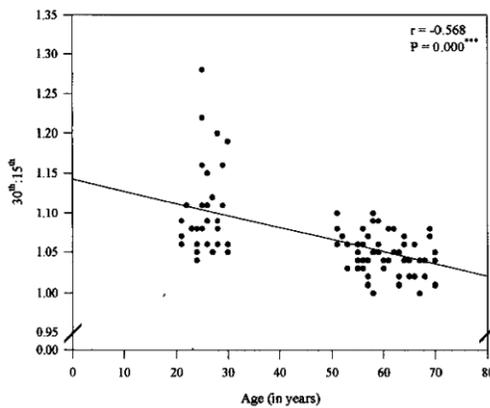
Pearson correlation-coefficient (r) test was performed as the test of significance. \*\*\* Significant at P<0.001

**Figure-1 :** Relationship between age and heart rate response to Valsalva maneuver (n=90)



Pearson correlation-coefficient (r) test was performed as the test of significance. \*\*\* Significant at P<0.001

**Figure -2:** Relationship between age and heart rate response to deep breathing



Pearson correlation-coefficient ( $r$ ) test was performed as the test of significance. \*\*\* Significant at  $P < 0.001$

**Figure -3:** Relationship between age and heart response to standing from lying.

#### Discussion:

In the present study the mean value of valsalva ratio was significantly lower in both elderly groups compared to that of adults. This finding is in agreement with other workers<sup>9, 12, 14-15, 22</sup>. Again, this ratio was lower in 61-70 years age group than that of 51-60 years but it was not statistically significant. No data is available to compare this finding.

Again, HR response to deep breathing was significantly lower in 51-60 years and 61-70 years than that of 21-30 years. Similar observation was made by other workers<sup>7, 15-16, 23-24</sup>. Again, significantly lower values of this H.R responses were also observed in 61-70 years compare to 51-60 years of elderly subjects. But no data is available to compare the finding.

Mean 30<sup>th</sup>:15<sup>th</sup> ratio was significantly lower in both 51-60 years and 61-70 years age groups than that of 21-30 years. Other workers also observed similar results<sup>7, 9-10, 14, 25</sup>. The mean measured value of this H.R response was also lower in 51-60 years than that of 61-70 years age group but it was not statistically significant. No data is available to compare the finding.

In this study, correlation of different parasympathetic nerve function parameters with age was analyzed. Here valsalva ratio, H.R response to deep breathing and 30<sup>th</sup>:15<sup>th</sup> ratio were negatively correlated with age and all these relationships were statistically highly significant. These findings are also similar with other workers<sup>9, 14</sup>.

The results of present study showed that impairment of parasympathetic nerve functions occurred in apparently healthy elderly subjects. Different investigators suggested that vagal tone is reduced or loss of vagal tone occurs gradually as age advances<sup>13, 27</sup>. Again, vagal damage causes reduction of heart rate to various stimuli<sup>5, 9</sup>. As a consequence, baroreflex activity may be decreased in old age. In addition, impaired transmission of impulse through both afferent and efferent pathway as well as reduced central integration of afferent inputs may be the contributory factors for this lower baroreflex activity in elderly subjects<sup>6, 18</sup>. All these explanations may be the cause of reduced parasympathetic nerve activity of elderly subjects in the present series, though the exact mechanism can not be elucidated from this study.

#### Conclusion

Therefore, considering the above features it may be concluded that aging process substantially impaired parasympathetic nerve functions.

#### Author Affiliations

- \*1. Assistant Professor, Medical College for Women & Hospital, Sector-1, Plot-4, Road-8/9, Uttara Model Town, Dhaka-1230.
2. Professor & Chairman, Department of Physiology, BSMMU, Shahbagh, Dhaka.
3. Professor, Department of Physiology, BSMMU, Dhaka.
4. Assistant Professor, Department of Physiology, BSMMU, Dhaka.
5. Assistant Professor, Department of Physiology, BSMMU, Dhaka.

*\*for correspondence*

## References

1. Latif SA, Hossain M, Hossain MS. Beginning to understand the human aging. *Mymensingh Med J.* 1999; 8(1): 64-69.
2. Esler MD, Tunner AG, Kaye DM. Aging effect on human sympathetic neuronal function. *Am J Physiol.* 1995; 264:278-85.
3. Francine GS, Cohn JN. Cardiac failure and the autonomic nervous system. In: Bannister SR, Mathias CJ editors. *Autonomic failure, A textbook of clinical disorders of the autonomic nervous system.* 3<sup>rd</sup> Edition. New York: Oxford University Press; 1992, 822-38 P.
4. Maser RE, Lenhard MJ, Pecherney GS. Cardiovascular autonomic neuropathy and the clinical significance of its determination. *J Endol.* 2000; 10:27-33.
5. Grubb BP. Syncope in the older patient. *Hellenic J cardiol.* 2003; 44: 235-42.
6. Jones PP, Christou DD, Jordan J, Seals DR. Baroreflex buffering is reduced with age in healthy men. *Circulation.* 2003; 107:1770-74.
7. Lipsitz LA. Syncope in the elderly. *Ann intern med.* 1983; 99:92-105.
8. Ingal TJ, McLeod JG, O'Brien PC. The effect of aging on autonomic nervous system function. *Aust NZ J Med.* 1990; 20 (4): 570-77.
9. O'Brien IAD, O'Hare P, Carrall KIM. Heart rate variability in healthy subjects: effect of age and derivation of normal ranges for test of autonomic function. *Br Heart J.* 1985; 55: 348-54.
10. Ewing DJ. Cardiovascular reflexes and autonomic neuropathy. *Clin Sci Mol Med.* 1978; 55: 312-27.
11. Shimada K, Kitazumi T, Hisakazu O, Sadakane N. Effect of age and blood pressure on the cardiovascular responses to the valsalva maneuver. *J Am Geriatr Soc.* 1986; 34:431-34.
12. Gautschi B, Weidmann P, Gnadinger MP. Autonomic function tests as related to age and gender in normal man. *J klin Wocherschr.* 1986; 64(11): 499-505.
13. Wieline W, Vanbrederode JEM, Derijk LG, Borst C, Dunning AJ. Reflex control of HR in normal subjects in relation to age, A data base for cardiac vagal neuropathy. *Diabetologia.* 1982; 22: 163-66.
14. Chu TS, Tasi TJ, Lai JS, Chen WY. Evaluation of cardiovascular autonomic function tests in normal subjects. *J Formosan Med Assoc.* 1989; 88:404- 06.
15. Smith SE, Smith SA. Heart rate variability in healthy subjects with a bedside computer based technique. *Clin Sci.* 1981; 61: 373-83.
16. Hellman JB, Stacy RW. Variation of respiratory sinus arrhythmia with age. *J Appl Physiol.* 1976 ; 41(5): 734-38.
17. Ewing DJ, Clarke BF. Diagnosis and management of diabetic autonomic neuropathy. *Br Med J.* 1982; 285:916-18.
18. Johnson RH. Aging and autonomic nervous system. In: Bannister SR, Mathias CJ. editors. *Autonomic failure, A textbook of clinical disorders of the autonomic nervous system.* 3<sup>rd</sup> ed. New York: Oxford university press; 1992, 882-903 p.
19. Mathias CJ, Bannister R. Investigation of autonomic disorders. In: Bannister SR, Mathias CJ, editors. *Autonomic failure, A text book of clinical disorders the autonomic nervous system.* 3<sup>rd</sup> ed. New York: Oxford university press; 1993, 255-90 p.
20. Cybulski G. Influence of age on the immediate cardiovascular response to orthostatic maneuver. *Euro J Appl physiol.* 1996 ; 73 (6):563-72.
21. Rajendra AU, Kannathal N, Sing OW, Png LY, Chua T. Heart rate analysis in normal subjects of various age groups. *J Biomed Engin.* 2004 ; 3 (24): 1-8.
22. Levin AB. A simple tests of cardiac changes induced by the valsalva maneuver. *Am J cardiol.* 1966; 18: 90-99.
23. Smith SA. Reduced sinus arrhythmia in diabetic autonomic neuropathy: diagnostic value of an age related normal range. *Br Med J.* 1982 ; 285:1599-1601.
24. Maddens M, Lipstiz LA, Wei JY, Pluchino FC, Mark P. Impaired heart rate response to cough. and deep breathing in elderly patients with unexplained syncope. *Am J cardiol.* 1987 ; 60:1368-72.
25. Dambrink JHA. Orthostatic regulation of blood pressure. A comparative study in young and old subjects. *Clin sci.* 1991 ; 81:51-58.
26. Mancia G, Ferrari A, Gregorini L, Parati G, Pomidossi G, Bertinieri G, Grassi G. Blood pressure and HR variability in normotensive and hypertensive human beings. *Circ Res.* 1983; 53: 96-104.
27. Shi X, Gallagher KM, O'Connor W, Foreman BH. Arterial and cardiopulmonary baroreflex in 60 to 69 vs 18 to 36 years old humans. *J Appl physiol.* 1996; 80: 1903-10.