HEART RATE PARTICULARITIES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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HEART RATE PARTICULARITIES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (Abstract): Autonomic nervous system dysfunction proved in chronic obstructive pulmonary disease (COPD) patients might determine an elevated cardiovascular risk by heart rate alteration. **Aim:** To assess the particularities of heart rate as a possible cardiovascular risk factor in COPD patients. **Materials and Methods:** This prospective, case-control study comparatively analyzed the pulse rate continuously recorded with a polygraph in 32 COPD patients and 29 healthy subjects during rest (supine and sitting position) and during submaximal exercise (6-minute walk test). The relation between pulse rate and respiratory, functional or clinical alterations was analyzed in COPD patients. **Results:** The mean pulse rate was significantly higher during rest and exercise in COPD patients compared with the controls. However, the chronotropic response determined by exercise was similar in COPD and control groups: 55.19 beats/minute and 57.21 beats/minute, respectively (p=0.686). The mean pulse rate during exercise correlated with hypoxemia (r=–0.354, p=0.47) and with resting pulse rate (r=0.871, p<0.001 for supine position). **Conclusions:** COPD associates elevated pulse rates during both rest and exercise. Hypoxemia and resting pulse rate are determinants of chronotropic response during submaximal exercise in COPD patients. **Keywords:** COPD, RESTING PULSE RATE, CHRONOTROPIC RESPONSE

One of the specific characteristics in COPD patients is represented by the presence of complex chronic comorbidities (1). Cardiovascular diseases represent important comorbidities, resulting in 26% of cause-specific mortality in COPD patients: 16% sudden death, 4% stroke, 3% myocardial infarction, 3% congestive heart failure (2). COPD associates an increased risk of developing acute cardiovascular events such as cardiac arrhythmia, deep vein thrombosis, pulmonary embolism, myocardial infarction, and stroke (3). However, the complex pathogenic relation between COPD and cardiovascular diseases is poorly understood, although there is evidence for the involvement of some common risk factors, such as smoking.

Patients with COPD have a lower heart rate recovery after exercise than healthy people. This alteration was proved as a strong predictor of mortality in COPD patients (4). Some researchers suggest that autonomic nervous system dysfunction
demonstrated in COPD patients may alter
the cardiac autonomic modulation and
subsequently the heart rate (5). These alter-
ations might partially explain the increased
cardiovascular risk in COPD patients. Giv-
en the pathogenic and prognostic implica-
tions of heart rate, our study aimed to as-
sess the particularities of heart rate as a
possible cardiovascular risk factor in
COPD patients.

MATERIAL AND METHODS

To achieve our goal we performed a
prospective, case-control study in which we
compared heart rate in COPD patients and
subjects without lung diseases.

The study included patients admitted to
the Iasi Clinic of Pulmonary Diseases in
the interval April 2011 - September 2012
diagnosed with COPD according to the
criteria in Global Initiative for Chronic
Obstructive Lung Disease (GOLD) guide-
lines: chronic dyspnea, cough, or sputum
production, and persistent airflow limi-
tation, confirmed by spirometry (a ratio of
forced expiratory volume in 1 second
(FEV1) to forced vital capacity (FVC) of
<0.7 after bronchodilator administration
(6). The control group included subjects
without history of lung diseases and with-
out clinical symptoms compatible with
COPD diagnosis or respiratory dysfunction,
according to the results of pulmonary func-
tion tests. COPD patients and controls were
matched for sex and age. Male gender and
age between 45 and 85 years were inclu-
sion criteria for both COPD and control
group. History of heart rhythm disorders
represented an exclusion criterion for both
COPD and control group.

The study protocol included clinical and
anthropometric assessment of the subjects:
body height and weight were measured and
body mass index (BMI) was calculated. The
degree of dyspnea was estimated for COPD
group using the Modified Medical Respira-
tory Council (MMRC) dyspnea scale (7). Health impairment in COPD patients was
measured by St George’s Respiratory Quest-
ionnaire (SGRQ). This provides three com-
ponent scores: symptoms, activity and im-
pacts scores, in addition to SGRQ total score
(8). Smoking history was expressed by the
number of pack-years (py). Pulmonary func-
tion was assessed by spirometry, including
postbronchodilator FEV1 measuring, to
confirm the diagnosis in COPD group. All
subjects underwent heart rate evaluation at
rest and during exercise (6-minute walk test,
6MWT). Using a polygraph (SOMNO-
check® Effort, Weinmann®, Germany), pulse rate and oxygen saturation (SpO2) were
continuously recorded as follows: 6
minutes with the patient in supine position,
6 minutes in sitting position and 6 minutes
during exercise (6MWT). The 6-minute
walk test was performed according to the
standards of American Thoracic Society (9).

The study was approved by the Ethics
Committee of Iasi Clinic of Pulmonary
Diseases, and the patients were enrolled
only after they provided appropriate in-
formed consent.

Data analysis was performed using Sta-
tistical Package for the Social Sciences
(SPSS v.16.0.). The data were presented as
mean ± standard deviation (SD). The equal-
ity of means for quantitative variables of
the control and COPD groups were as-
essed for significance using the unpaired
Student’s t-test. In case the assumption of
normality was not met, a nonparametric
test was applied (Mann–Whitney U-test).
Analysis of variance (ANOVA) was used
to test the means equality in case of more
than two samples. The Pearson correlation
coefficient or the Spearman rank correla-
tion coefficient was calculated to assess the
relationships between various clinical and functional parameters in COPD patients. All statistical tests were 2-tailed, and p values < 0.05 were considered significant for all analyses.

RESULTS
We enrolled a total of 32 patients in the COPD group and 29 subjects in the control group. The COPD group had a higher smoking index and a lower body mass index than the control group. The 6-minute walking distance was significantly higher for the control group (tab. I).

Regarding pulse rate, both case and control groups shared a similar trend, the mean values significantly increasing from supine to sitting position and from sitting position to exercise during 6MWT (p<0.001 for both COPD and control groups). The results demonstrate significantly higher pulse rate mean values in COPD subjects than in controls, during rest as well as during exercise: supine position, sitting position and 6-minute walk test, respectively (tab. II, fig. 1). However, no significant differences were found between study groups in pulse rate increase (mean pulse rate differences) from supine to sitting position (p=0.479) and from sitting position to exercise during 6MWT (p=0.065).

### TABLE I

<table>
<thead>
<tr>
<th>Subjects n</th>
<th>COPD</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=32</td>
<td>n=29</td>
<td></td>
</tr>
<tr>
<td>Age yrs</td>
<td>65.75 ± 8.79</td>
<td>61.72 ± 8.51</td>
</tr>
<tr>
<td>Weight kg</td>
<td>68.09 ± 17.48</td>
<td>83.37 ± 15.93</td>
</tr>
<tr>
<td>Height cm</td>
<td>168.59 ± 7.27</td>
<td>171.17 ± 5.75</td>
</tr>
<tr>
<td>BMI kg·m⁻²</td>
<td>23.81 ± 5.18</td>
<td>28.37 ± 4.79</td>
</tr>
<tr>
<td>Smoking py</td>
<td>38.64 ± 19.43</td>
<td>17.96 ± 20.13</td>
</tr>
<tr>
<td>MMRC</td>
<td>2.28 ± 0.95</td>
<td>17.96 ± 20.13</td>
</tr>
<tr>
<td>FEV₁</td>
<td>38.9 ± 13.5</td>
<td>102.5 ± 14.8</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>52.6 ± 11.1</td>
<td>80.7 ± 7.3</td>
</tr>
<tr>
<td>6MWT m</td>
<td>281.4 ± 107.5</td>
<td>426 ± 77.4</td>
</tr>
</tbody>
</table>

### TABLE II

<table>
<thead>
<tr>
<th>Subjects n</th>
<th>COPD</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=32</td>
<td>n=29</td>
<td></td>
</tr>
<tr>
<td>Pulse rate beats·min⁻¹</td>
<td>Mean ± SD</td>
<td>Min</td>
</tr>
<tr>
<td>Supine</td>
<td>78.16 ± 16.61</td>
<td>52.2</td>
</tr>
<tr>
<td>Sitting</td>
<td>82.67 ± 17.03</td>
<td>52.7</td>
</tr>
<tr>
<td>6MWT</td>
<td>97.07 ± 2.36</td>
<td>90.1</td>
</tr>
</tbody>
</table>
Heart rate particularities in chronic obstructive pulmonary disease

Fig. 1. The trend of pulse rate in the study groups

Even if pulse rate increase seems to be higher in controls than in COPD group as a result of the transition from rest to exercise (6MWT), the difference was on the borderline of statistical significance. The resting pulse rate (mean pulse rate for supine position) and peak pulse rate (maximum value during 6MWT) were assessed, the calculated difference between peak rate and resting rate representing the chronotropic response to exercise. The chronotropic peak moment was determined as the time of the peak in pulse rate during the 6 minute period of walk test. The chronotropic response and the chronotropic peak moment did not show significant differences between COPD and control groups (tab. III).

| TABLE III |
| Chronotropic response – comparison between COPD and control groups |

| Subjects n | COPD | Control |
| n=32 | n=29 |
| Pulse rate variation beats·min⁻¹ | Mean ± SD | Mean ± SD | p value |
| Supine to sitting | 4.71 ± 8.49 | 5.07 ± 4.6 | 0.479 |
| Sitting to 6MWT | 14.25 ± 8.58 | 19.1 ± 11.47 | 0.065 |
| Chronotropic response (beats·min⁻¹) | 55.19 ± 30.93 | 57.21 ± 26.39 | 0.686 |
| Chronotropic peak moment (sec) | 173.9 ± 114.7 | 181.9 ± 111.3 | 0.783 |
We searched for potential determinates of pulse rate alterations in COPD patients, assessing the relation of this parameter with other clinical or functional parameters (tab. IV). The mean pulse rate during 6 minute walk test inversely correlated with mean SpO2. In COPD patients, SpO2 demonstrated an opposite trend than pulse rate in relation with exercise, significantly decreasing during walk test as compared with rest in supine position (p=0.019). However, we did not find other correlations between pulse rate alteration, either during rest or exercise, and any other functional or clinical parameter in COPD patients, including MMRC dyspnea score, FEV1 and SGRQ scores. Resting pulse rate seems to determine the pulse rate increase during exercise, 6MWT mean pulse rate strongly correlating with mean pulse rates for both supine and sitting position (p<0.001).

### TABLE IV
Potential determinatives for the pulse rate alteration in COPD group

<table>
<thead>
<tr>
<th></th>
<th>Correlation coefficient r</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine pulse rate</td>
<td>Sitting pulse rate</td>
<td>0.871</td>
</tr>
<tr>
<td>Supine pulse rate</td>
<td>6MWT pulse rate</td>
<td>0.701</td>
</tr>
<tr>
<td>Sitting pulse rate</td>
<td>6MWT pulse rate</td>
<td>0.819</td>
</tr>
<tr>
<td>6MWT pulse rate</td>
<td>6MWT SpO2</td>
<td>-0.354</td>
</tr>
</tbody>
</table>

**DISCUSSION**

COPD associates an important risk of cardiovascular disease, the factors responsible for this association remaining largely unknown. Elevated resting heart rate was proved to be a strong independent risk factor for cardiovascular diseases in healthy subjects (10).

Our results have proved a significantly higher resting heart rate in COPD patients compared with controls without lung disease, for either supine or sitting position. Jensen et al. showed that resting heart rate was associated with cardiovascular mortality in a study including 16,696 COPD patients. They also found a strong association of the resting heart rate with COPD severity assessed as airway obstruction (11). We did not find any association between resting heart rate and FEV1 percent of predicted value (p=0.54), probably because of the small size of our study group. Furthermore, Van Gestel et al. found a significant correlation between resting heart rate and exercise capacity assessed by 6MWT distance (12). Our study did not prove any association between resting heart rate and health impairment measured by SGRQ in COPD patients in either symptoms, activity, impacts, or total scores of SGRQ. Dyspnea score (MMRC) did not correlate with resting heart rate, too. The higher resting heart rate might be explain by autonomic nervous system dysfunction in COPD patients, resulting in alterations of cardiac autonomic modulation and enhanced sympathetic tone at rest (5). Hypoxemia seems to be one of the determinant factors of this dysfunction, given the effect of oxygen supplementation which significantly and favorably alters autonomic modulation in COPD (13). There are also studies which obtained divergent results. Chen et al. found that resting autonomic nervous function of COPD patients is not different from that of normal controls.

The airway obstruction was not related
Heart rate particularities in chronic obstructive pulmonary disease

to the cardiac autonomic nervous function, but a worse oxygenation status was associated with increased cardiac vagal and decreased cardiac sympathetic activities in COPD patients (14).

Most of the researches regarding resting heart rate in COPD have assessed the patients in supine position. However, the transition from supine to sitting position is proved to improve hemodynamics, to decrease the respiratory functional residual capacity and airflow limitation, and to allow the accessory muscle use in breathing (15). These functional mechanisms which explain the orthopnea in COPD as well as in heart failure may also result in autonomic modulation and consequently in heart rate modulation. We found a significant increase in heart rate determined by transition from supine to sitting position in COPD patients. The heart rate increase in COPD patients was similar with the heart rate increase in healthy subjects (4.71 beats/minute and 5.07 beats/minute, respectively). However the mean heart rate for sitting position was significantly higher in COPD patients than in the control group subjects, maintaining the same trend as in supine position. The exercise represented by 6MWT determined a similar chronotropic response in COPD group compared with control group (55.19 beats/minute and 57.21 beats/minute, respectively). However, the mean heart rate during exercise was significantly higher in COPD patients than in controls, maintaining the same trend as at rest. The mean time for chronotropic peak reaching, within the 6 minute period was also similar in COPD and control groups (173.9 seconds and 181.9 seconds, respectively). Our results on heart rate assessment during exercise are different from the results obtained by Inal Ince et al. They found a peak heart rate and chronotropic index significantly lower in COPD patients than in healthy subjects (p<0.05). Other interesting finding in their study was the relation between chronotropic response, BMI, and dyspnea score (MMRC), respectively. Weight and body mass index were significantly higher than in COPD patients with normal chronotropic response (p<0.05). MMRC dyspnea score explained 44% of the variance in chronotropic index (16). We did not find any correlations between chronotropic response and functional or clinical parameters in COPD patients, including MMRC dyspnea score, FEV1 and SGRQ scores. However, we determined the chronotropic response during a submaximal exercise test (6MWT), unlike the study by Inal Ince et al. who used incremental exercise testing, although the COPD group in their study included only 25 patients.

The results obtained by Bartels et al. suggest that cardiac autonomic modulation is altered in patients with COPD during maximal exercise. Autonomic changes were not significantly correlated with age, gender, body mass index, spirometry, lung volumes, resting gas exchange, or oxygen saturation during exercise (17). In our study, oxygen saturation and resting pulse rate seemed to be the only possible determinates of pulse rate increase during submaximal exercise, strongly correlating with the mean pulse rate during 6MWT.

**CONCLUSIONS**

COPD associates elevated pulse rates during both rest and exercise. Pulse rate increasing in transition from supine to sitting position and chronotropic response during exercise are similar in COPD and healthy subjects. Hypoxemia and resting pulse rate are determinates of chrono-
tropic response during exercise in COPD patients. Pulse rate alterations do not correlate with airway obstruction, dyspnea, or health impairment in chronic obstructive lung disease. Although more data are needed, elevated heart rate associated during both rest and exercise might result in increased cardiovascular risk in COPD.

ACKNOWLEDGEMENTS
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REFERENCES


