Relationship between exercise test recovery indices and psychological and quality-of-life status in hemodialysis patients: a pilot study

Anastasia P. Samara 1, Evangelia Kouidi 1, Stavroula Ouzouni 1, Stylianos Vasileiou 2, Athanasios Sioulis 2, Asterios Deligiannis 1

1 Sports Medicine Laboratory, Department of Physical Education and Sports Science, Aristotle University of Thessaloniki, Thessaloniki - Greece
2 Internal Medicine Clinic A - Renal Unit, Aristotle University of Thessaloniki, Thessaloniki - Greece

ABSTRACT

Background: The aim of this study was to correlate the psychological and health-related quality-of-life status of hemodialysis (HD) patients with recovery indices following maximal and submaximal exercise tests.

Methods: Twenty patients on HD (aged 53.5 ± 12.9 years) and 18 healthy individuals (aged 54.1 ± 10.2 years) underwent a maximal and a submaximal cardiopulmonary test (CPETmax and CPETsubmax). Heart rate recovery (HRrec) 1 minute after exercise and time for VO2 to decrease by half (T1/2VO2) were determined. All subjects also completed 3 questionnaires: (a) the Beck Depression Inventory (BDI), (b) Quality of Life Index (QLI)–Spitzer Index and (c) SF-36 physical and mental component summary scales.

Results: HRrec after maximal (p=0.029) and submaximal test (p=0.041) was found to be lower in patients compared with healthy individuals. T1/2VO2 was raised by 29% (p=0.003) in patients compared with controls. Moreover, a significantly higher BDI (by 133.7%), lower SF-36 physical (by 47.8%) and mental (by 42.9%) component summary score and lower QLI (by 32.1%) results were found in HD patients compared with controls. BDI (p=0.045), QLI (P=0.011), SF-36 physical (p=0.017) and mental component scales (p=0.021) were independently associated with HRrec in maximal tests in patients. Similar correlations remained for submaximal tests among HRrec and BDI (p=0.004), QLI (p=0.006), SF-36 physical (p=0.048) but not mental scales (p=0.369) in the patients’ group. T1/2VO2 also correlated to BDI (p=0.019), QLI (p=0.005) and SF-36 mental scale (p=0.017) in maximal tests in these patients. In contrast, there was a correlation between HRrec and BDI (p=0.004) in the control group for maximal tests only.

Conclusions: In conclusion, in HD patients, recovery indices following maximal and submaximal exercise tests were shown to provide useful indications of the patients’ psychological and quality-of-life profiles.

Key words: Depression, Dialysis, Maximal and submaximal cardiopulmonary tests, Quality of life, Recovery indices

INTRODUCTION

Heart rate recovery (HRrec) reflects cardiac parasympathetic activation, both in healthy individuals and chronic patients (1, 2). Moreover, it has been shown to be an efficient predictor of psychological distress and overall mortality in healthy individuals and patients with chronic heart failure (CHF) (3-5). HRrec is measured 1 minute after exercise termination, after maximal (CPETmax) or submaximal cardiopulmonary exercise testing (CPETsubmax). Both tests are widely accepted as objective methods to grade functional status in healthy individuals and chronic patients (6-8). Moreover, recent studies in CHF patients report that CPETsubmax recovery indices, such as HRrec and time required for VO2peak to decrease by half (T1/2VO2), significantly correlate to correspondences of CPETmax and can be used as indicators of patients’ daily activities (9, 10).

Depression and poor quality of life are the most common psychological disorders in chronic hemodialysis (HD) patients, with a prevalence rate of over 50% (11). Several investigators have reported the interaction of psychosocial distress with bad outcomes; thus, increased levels of depression and poor quality of life have been associated with increased morbidity and mortality in HD patients (12-14). Moreover, depressive symptoms have been associated with
alterations of the cardiac autonomic function, as increased sympathetic or decreased vagal activity (15).

It is well known that HD patients demonstrate evidence of cardiac autonomic dysfunction (16, 17). As a result of this dysregulation, HD patients may experience higher incidences of cardiac arrhythmias and adverse cardiac events (18).

To date, no study has focused on the comparison of the recovery parameters mentioned, deriving from either maximal or submaximal exercise testing, with psychosocial profiles of HD patients. Therefore, the aim of this pilot study was to test the correlation between recovery indices ($HR_{rec}$ and $T_{1/2}VO_2$) after maximal and submaximal exercise tests, and depression and quality-of-life status in these patients.

**METHODS**

**Subjects**

Twenty patients (15 men) who underwent HD 3 times a week for at least 6 months in the Renal Unit of the AHEPA University Hospital in Thessaloniki, Greece, volunteered to participate in this pilot study (group A). Patients with no evidence of myocardial infarction within 1 year, or severe arrhythmias, uncontrolled hypertension, diabetes, neurologic disorder with functional deficit or musculoskeletal limitation were included. Moreover, patients were selected for the trial if they had a hemoglobin level within the range of 10-12 g/dL. All patients were on a stable medication regimen and received no antidepressants or other psychotropic agents and/or medication (β-blockers or antiarrhythmics) that could affect their autonomic nervous system. Eighteen healthy age- and gender-matched individuals (14 men) were used as controls (group B). The study was in adherence with the Declaration of Helsinki and the recommendations of the university ethics committee. Moreover, informed consent was obtained from all participants.

**Measures**

**Cardiopulmonary exercise testing**

All tests were performed between 10:00 AM and 13:00 PM, on a nondialysis day. Subjects were asked to refrain from caffeine-containing beverages for at least 2 hours prior to tests. The participants underwent a symptom-limited maximum cardiopulmonary exercise test (CPET$_{max}$) on a treadmill (Trackmaster TM-400), according to Bruce protocol. On the third day, they performed a 6-minute cardiopulmonary exercise test at submaximal intensity (CPET$_{submax}$) at each individual’s ventilatory threshold (Vt), at the speed and grade at which the Vt was achieved on the CPET$_{max}$. The Vt was determined as systematic rise of VE/VO$_2$ ratio without further rise in VE/VCO$_2$ and was identified independently by 2 experienced investigators (19).

During the tests, expired air was collected in a face mask and analyzed on a breath-by-breath basis for quantification of oxygen consumption (VO$_2$), minute ventilation (VE), ventilatory equivalents for oxygen (VE/VO$_2$) and carbon dioxide (VE/VCO$_2$), and respiratory exchange ratio (VCO$_2$/VO$_2$) with the use of the ergospirometer MedGraphics Breeze Suite CPX Ultima (Medical Graphics, St. Paul, MN, USA). Peak VO$_2$ was defined as the highest VO$_2$ level obtained when the respiratory exchange ratio was greater than 1.10. After achieving a peak workload, the treadmill was stopped, and patients were asked to sit down without a “cool down” period. Indications to stop the CPET$_{max}$ were exhaustion (according to Borg’s scale), dyspnea, angina, ST-segment depression >2 mm or systolic blood pressure >260 mm Hg or and diastolic >100 mm Hg, as well as a progressive decrease in blood pressure. A 12-lead electrocardiogram (CH-200; Cambridge Heart Inc, Bedford, MA, USA) was continuously monitored in both tests. Blood pressure was also recorded at baseline, every 3 minutes during exercise and during recovery, by a cuff sphygmomanometer.

Heart rate was measured at rest, every 3 minutes during exercise, at peak and every minute during recovery. $HR_{rec}$ was defined as maximum HR minus HR at the first minute of passive recovery, and represented the drop in HR during that time interval. Additionally, time required for oxygen uptake to decrease by half ($T_{1/2}VO_2$) after termination of maximum exercise was calculated. Other parameters also measured were VE/VCO$_2$ and VE/VO$_2$ at peak exercise, total exercise time and time required to reach Vt. In the submaximal exercise test, HR$_{rec}$, VE/VCO$_2$ and VE/VO$_2$ were also measured.

**Psychological, quality-of-life and health status assessment**

Subjects were asked to answer, self-administered, the following 3 questionnaires after clear instructions:

(i) The Beck Depression Inventory (BDI), as translated and standardized for the Greek population, which is a self-rating questionnaire for the assessment of the severity of depression. It is composed of 21 items, each with a 0-3 grading system. Each item consists of 4 self-evaluative statements of increasing severity. A total score of 0-9 indicates no depression, 10-15 mild to moderate depression, 16-23 moderate to severe depression, and a score ≥24 indicates severe depression (20, 21).
(ii) The Quality of Life Index (Spitzer Index; QLI), also translated for the Greek population, a questionnaire with 5 domains measuring patient’s activity, daily living, health, support and outlook (22).

(iii) The Short Form-36 questionnaire (SF-36), a multipurpose, short-form health survey with 36 questions, which yielded an 8-scale profile of scores as well as physical component summary (PCS) and mental component summary (MCS) scores. Scores range from 0 to 100, with 100 representing the best perceived quality of life. It has also been translated and standardized for the Greek population (23).

Statistical analysis

Data are reported as means ±SD. An independent samples t-test was used to assess differences between groups. Pearson’s correlation coefficient was used to estimate the univariate relationship between 2 variables. Linear regression analysis was used to test the relationship between psychological factors and physiological indices after CPET\textsubscript{max} and CPET\textsubscript{submax}, independent of covariates. All statistical analyses were performed using SPSS 12.0 for Windows (Statistical Package for Social Sciences Inc., Chicago, IL, USA). A p value <0.05 was considered statistically significant.

RESULTS

The clinical characteristics of HD patients and healthy individuals are presented in Table I. There were no differences in age, height, weight and body surface area between groups. Table II shows the data for CPET\textsubscript{max} and CPET\textsubscript{submax} in HD patients and healthy volunteers. During CPET\textsubscript{max}, patients had a 17.9% (p<0.001) lower heart rate at peak exercise, and a 32% lower VO\textsubscript{peak} than healthy individuals (p<0.001). Time to reach ventilatory threshold and total exercise time were lower by 48% (p=0.001) and 35% (p<0.001) in group A compared with group B, respectively. Conversely, healthy individuals reached lower levels of VE/VCO\textsubscript{2} by 27.3% (p=0.002) and of VE/VO\textsubscript{2} by 26.8% (p=0.001), respectively, than HD patients. Finally, during recovery, patients had 24.4% lower HR\textsubscript{rec} (p=0.029) and a 27% higher T\textsubscript{1/2}VO\textsubscript{2} (p=0.003) compared with controls.

There was no significant difference in peak heart rate during CPET\textsubscript{submax} between groups. However, group A had a 21% lower HR\textsubscript{rec} (p=0.041) and higher levels of ventilatory equivalents for oxygen (by 23.3%; p=0.001) and carbon dioxide (by 30.4%; p<0.001) compared with controls.

Data for psychological profiles and scores for health-related quality-of-life indices are presented in Table III. Eighteen patients (90%) had moderate to severe depression ≥16. Mean

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>CLINICAL CHARACTERISTICS OF PATIENTS (GROUP A) AND CONTROLS (GROUP B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GROUP A</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>15/5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.5 ± 12.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170 ± 9.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.2 ± 11.5</td>
</tr>
<tr>
<td>BSA (m\textsuperscript{2})</td>
<td>1.88 ± 0.19</td>
</tr>
<tr>
<td>BMI (calculated as kg/m\textsuperscript{2})</td>
<td>25.2 ± 2.7</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>11.1 ± 0.9</td>
</tr>
<tr>
<td>Years on HD</td>
<td>6.2 ± 4.3</td>
</tr>
<tr>
<td>Frequency of HD (times/week)</td>
<td>3</td>
</tr>
<tr>
<td>Duration of HD (hours)</td>
<td>4</td>
</tr>
</tbody>
</table>

Values expressed as means ± SD, or number.

BMI = body mass index; BSA = body surface area; Hb = hemoglobin; HD = hemodialysis.
TABLE II
MAXIMAL (CPETmax) AND SUBMAXIMAL (CPETsubmax) CARDIOPULMONARY EXERCISE TESTS IN PATIENTS (GROUP A) AND CONTROLS (GROUP B)

<table>
<thead>
<tr>
<th>CPET max</th>
<th>Index</th>
<th>Group A</th>
<th>Group B</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRrest (beats/min)</td>
<td>77.5 ± 11.9</td>
<td>75.1 ± 7.5</td>
<td>0.448</td>
<td></td>
</tr>
<tr>
<td>Peak exercise index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak heart rate (beats/min)</td>
<td>137.3 ± 18.9</td>
<td>165.5 ± 14.6</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>VO2peak (ml/kg/min)</td>
<td>22.6 ± 3.8</td>
<td>31.6 ± 6.4</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>VT (seconds)</td>
<td>149.8 ± 59.3</td>
<td>261.2 ± 112.4</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Exercise time (seconds)</td>
<td>437 ± 118.6</td>
<td>637.7 ± 140.9</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>35.3 ± 5.3</td>
<td>29.5 ± 2.0</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>VE/VO2</td>
<td>38.2 ± 4.5</td>
<td>31.8 ± 4.0</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Recovery index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRrec (beats at 1 minute)</td>
<td>18.8 ± 5.8</td>
<td>23.8 ± 7.3</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td>T1/2VO2 (seconds)</td>
<td>127 ± 35.1</td>
<td>98.1 ± 19.1</td>
<td>0.003</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CPET submax</th>
<th>Index</th>
<th>Group A</th>
<th>Group B</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak exercise index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak heart rate (beats/min)</td>
<td>113.5 ± 18.7</td>
<td>116.3 ± 10.0</td>
<td>0.561</td>
<td></td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>31.8 ± 4.1</td>
<td>27.0 ± 2.5</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>VE/VO2</td>
<td>32.1 ± 5.3</td>
<td>24.9 ± 2.3</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Recovery index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRrec (beats at 1 minute)</td>
<td>14.7 ± 6.0</td>
<td>18.6 ± 5.2</td>
<td>0.041</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD.
HRrest = heart rate at rest; VO2peak = peak oxygen consumption; VT = ventilatory threshold; VE/VCO2 = ventilatory equivalents for carbon dioxide; VE/VO2 = ventilatory equivalents for oxygen; HRrec = heart rate recovery; T1/2VO2 = time required for VO2peak to decrease by half.

BDI score in group A was 115.4% greater (p<0.001) compared with that in group B. In contrast, QLI scores were 24.2% lower (p<0.001) in group A compared with group B. Finally, healthy individuals reached higher levels of PCS scores (by 46.4%; p<0.001) and MCS scores (by 37.8%; p<0.001) on the SF-36 questionnaire compared with the patients’ group. Pearson’s correlations between cardiopulmonary indices after maximal and submaximal testing and psychological parameters are presented below. All data of these physiological parameters, such as HRrec for both tests and T1/2VO2 in the CPETmax test, were found to be significantly correlated with BDI and QLI in HD patients. Specifically, in the CPETmax, BDI correlated to HRrec (r = −0.454; p = 0.045) and T1/2VO2 (r = 0.518; p = 0.019). In the CPETsubmax, a similar correlation was found between BDI and HRrec (r = −0.609; p = 0.004). QLI results were highly correlated to all indices in both tests – that is, to HRrec (r = 0.558; p = 0.011) and T1/2VO2 (r = −0.603; p = 0.005) in the CPETmax and to HRrec (r = 0.596; p = 0.006) in the CPETsubmax. As for the SF-36 test, there was no pattern in correlation with recovery indices. PCS scores correlated with HRrec (r = 0.525; p = 0.017) in the CPETmax and HRrec (r = 0.448; p = 0.048) with the CPETsubmax, and MCS scores with HRrec (r = 0.511; p = 0.021) and T1/2VO2 (r = −0.526; p = 0.017) only in the CPETmax. No similar correlation was found in controls. Furthermore, HRrec of patients after CPETmax correlated highly to HRrec in the CPETsubmax (r = 0.447; p = 0.048).
Additionally, VO\textsubscript{2peak} correlated to BDI ($r = -0.447; p=0.048$), to QLI ($r = 0.791; p<0.001$), to SF-36 PCS ($r = 0.730; p<0.001$) but not to SF-36 MCS ($r = 0.376; p=0.102$).

Additionally, in the CPET\textsubscript{max}, there was a correlation between HR\textsubscript{rec} and VO\textsubscript{2peak} ($r = 0.571; p=0.009$) and $T_{1/2}$VO\textsubscript{2} ($r = -0.464; p=0.039$) of patients. In CPET\textsubscript{submax}, HR\textsubscript{rec} was also correlated to VO\textsubscript{2peak} ($r = 0.599; p=0.005$) and was close to $T_{1/2}$VO\textsubscript{2} ($r = -0.426; p=0.061$).

### DISCUSSION

The main finding of this pilot study was that cardiopulmonary recovery indices after exercise testing, both for maximal and submaximal efforts, were correlated to levels of depression and quality of life in HD patients. To our knowledge, no study has investigated the relation of postexercise recovery physiological parameters and psychosocial status in these patients.

Dialysis patients often experience psychological distress (11, 12, 24-26). Depression has been also associated with impaired quality of life in these patients and is a marker of poor outcomes (13, 27, 28). Similarly, our patients displayed moderate to severe depression symptoms. Accordingly, QLI and SF-36 scores were significantly lower in our patients in comparison with healthy volunteers. Similar results were described previously in these patients (13, 26, 29). Moreover, depression has been shown to be correlated to decreased cardiorespiratory fitness, which may be the consequence of a lower engagement of individuals in physical activity (14). A number of factors are suggested as potential mechanisms responsible for the negative effect of depression on prognosis and secondary outcomes in chronic disease patients, which include biological processes (elevated sympathetic tone, increased levels of catecholamines, inflammation) and adverse health behaviors (lack of physical activity, noncompliance to pharmacological regimens, poor dietary control and smoking) (30). A similar positive relationship between depression and HD patients’ aerobic capacity and cardiac autonomic dysfunction was described previously (15, 29). Interestingly, the improvement of aerobic capacity and sympathovagal balance following exercise training had beneficial effects on the psychological status of these patients (29).

During maximal cardiopulmonary exercise testing, HD patients achieved a shorter exercise time and a lower peak oxygen uptake and ventilatory threshold compared with healthy volunteers. Low VO\textsubscript{2peak} values, ranging from 15 to 25 ml/kg/min, have been also reported in previous studies (31, 32). A number of potential mechanisms are proposed to explain the poor aerobic capacity of HD patients, both central and peripheral, including cardiac dysfunction, anemia, muscular atrophy, metabolic disorders, decreased cardiac response to exercise, deconditioning and others (33-35). Peak oxygen uptake (VO\textsubscript{2peak}) has been proven to be a powerful predictor of health outcomes in HD patients (36). However, exertion to the point of exhaustion is not always achievable in HD patients. They are often forced to early termination due to early fatigue or discomfort (37). A submaximal stress ECG test, such as a 6-minute walking test, can be a useful alternative tool in evaluating functional parameters of HD patients in clinical practice, similar to what is used for cardiac patients (38, 39). After the CPET\textsubscript{submax}, HR\textsubscript{rec} and ventilatory equivalents for oxygen and carbon dioxide followed the same pattern as in the CPET\textsubscript{max}. Thus, our findings confirm the positive correlation between a maximal and a submaximal test, as reported previously (8).

---

**TABLE III**

| PSYCHOLOGICAL PROFILES AND SCORES FOR HEALTH-RELATED QUALITY-OF-LIFE INDICES IN PATIENTS (GROUP A) AND CONTROLS (GROUP B) |
|---|---|---|
| **Group A** | **Group B** | **Group C** |
| BDI | 19.4 ± 3.6 | 8.3 ± 0.9 | 0.000 |
| Quality-of-Life Index | 6.7 ± 1.7 | 8.6 ± 0.9 | 0.000 |
| SF-36 | | | |
| PCS | 39.5 ± 3.8 | 75.6 ± 3.5 | 0.000 |
| MCS | 38.9 ± 7.4 | 68.2 ± 4.3 | 0.000 |

BDI = Beck Depression Inventory questionnaire; PCS = physical component summary score; MCS = mental component summary score.
Postexercise functional indices, such as HR_{rec} and T_{1/2}VO2, after maximal exercise, were found to be depressed in HD patients, compared with healthy subjects. These results may be explained by impaired parasympathetic activity reported in these patients (35). Lower HR_{rec} after exercise is associated with several negative health outcomes in cardiac patients, including impaired fibrinolysis, increased cardiopulmonary resuscitation, carotid atherosclerosis and arterial stiffness (40-43). Interestingly, HR_{rec} is a predictor of incident diabetes mellitus, metabolic syndrome and, ultimately, of mortality (30, 44). Moreover, the slower return of oxygen uptake after the end of exercise (T_{1/2}VO2), in comparison with healthy individuals, was attributed to a slowed replenishment of energy stores in peripheral muscles (9). This slower recovery of muscle energy stores, seemingly independent of the patient's exercise level, has been attributed to histologic and biochemical muscle alterations, impaired O2 delivery to skeletal muscles during recovery, and vascular dysfunction in patients with CHF (9, 45).

Our results demonstrated that depression was significantly associated with HR_{rec} and T_{1/2}VO2 after maximal testing, as well as HR_{rec} after submaximal testing. Accordingly, impaired QLI was also associated with T_{1/2}VO2 in the CPET_{max} test and attenuated HR_{rec} in both the CPET_{max} and CPET_{submax}. Interestingly, the physical component summary scores of the SF-36 but not the mental component summary scores were significantly associated with reduced HR_{rec}. Significant positive relationships between HR_{rec} and psychological distress and impaired quality of life have been described in cardiac patients (4, 5). It is suggested that there is an interaction of psychological factors with cardiac autonomic dysregulation in these patients (4, 5).

Results of this pilot study must be interpreted in the face of certain limitations. It has not yet been clarified to what extend cardiac autonomic dysregulation in HD patients occurs because of cardiac, renal or other factors. Thus, the relationship between cardiopulmonary recovery indices and psychological profiles may be in part attributed to cardiac autonomic dysfunction; however, this parameter has not been examined in the present study. Additionally, we cannot draw conclusions about the effect of decreased recovery indices on total morbidity outcome in these patients. Finally, an interesting relationship between recovery indices, even at submaximal intensity, and psychological and quality-of-life status in these patients was suggested. However, the links between exercise capacity, cardiac autonomic function and psychosocial profiles of HD patients should be examined further in future studies.

Financial support: There was no financial support for this study.

Conflict of interest statement: The authors declare no conflict of interest with regard to the present work.

Address for correspondence: Anastasia P. Samara, MSc
28 K. Koun Street
GR-566 26 Thessaloniki, Greece
ansamara@phed.auth.gr

**REFERENCES**


Accepted: February 22, 2012