Prospective Clinical Research Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
48(1) 1–9

DOI: 10.1177/0300060519898008
journals.sagepub.com/home/imr
SAGE

Effect of physical activity on depression symptoms in patients with IgA nephropathy

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Abstract

Objective: We aimed to assess the effects of physical activity (PA) on depression symptoms in patients with IgA nephropathy (IgAN).

Methods: We developed a 6-month personalized PA training program for patients with IgAN. At the beginning and after completion of the training intervention, patients' cardiopulmonary function was assessed via a spiroergometric study. Prior to the start of and after the intervention, we administered the Beck Depression Inventory-II (BDI-II), Eysenck Personality Questionnaire (EPQ), Quality of Life Index (QLI), Life Satisfaction Index, and Short Form-36 (SF-36) to all participants. Scores of the QLI were used as the dependent variable.

Results: A total of 216 patients were included in our analysis. After completing the PA training program, cardiopulmonary function and depressive symptoms were significantly improved in patients with IgAN, as compared with baseline values. Multiple logistic regression analysis showed that regular PA; extended hemodialysis interval; decreased scores of the BDI-II, EPQ, and SF-36 Mental Component Scale; and increased SF-36 Physical Component Scale scores were independently associated with improved QLI.

Conclusions: Regular PA may improve cardiopulmonary function, depression symptoms, and health-related quality of life in patients with IgAN.

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Keywords
Physical activity, depression, IgA nephropathy, quality of life, training program, cardiopulmonary function

Date received: 23 September 2019; accepted: 10 December 2019

Introduction

IgA nephropathy (IgAN) is the most common primary glomerular disease worldwide, accounting for approximately 30% to 40% of cases of primary glomerular disease.[1] IgAN is a progressive disease, with about 10% of patients progressing to chronic renal failure within 10 years after diagnosis. IgAN is the primary disease associated with chronic maintenance hemodialysis.[2,3] Most patients do not fully understand the cause, pathogenesis, and treatment of IgAN, and many other factors can cause mental stress in patients with IgAN, such as decreased ability to work and perform activities of daily living, leading to high economic pressure and limited social activities.[4]

Depression is a modern social epidemic, with high incidence but also high levels of concealment of the disorder. Depression is defined as a persistent state of low mood, and the specific causes of disease are complex.[5] Depression is generally believed to be related to "loss", such as loss of kidney function, loss of health, loss of status in family and work units, loss of economic resources and sexual function.[6] Several factors cause the incidence of depression to be significantly higher in patients with chronic kidney disease (CKD) than that in the normal population; such factors include a high economic burden and physical pain owing to long-term maintenance hemodialysis, which can prevent patients from participating in normal social activities owing to long-term hospitalization and dietary restrictions.[7]

Patients with IgAN often face greater stress in their daily life, so they generally have a greater tendency to experience negative emotions. Related studies have reported that depression levels are closely related to poor quality of life and that physical activity (PA) can alleviate the mental stress of patients with CKD.[8–10] However, there are very few studies investigating the effects of regular PA on the mental state and quality of life in patients with IgAN. Therefore, the purpose of this study was to assess the improvement in levels of depression among patients with IgAN who engage in regular PA and to clarify the relationship between PA and improvement in quality of life.

Methods

Study population

We conducted a prospective observational study at Ningbo Urology and Nephrology Hospital from September 2013 to August 2018. The inclusion criteria for the current study were 1) adults (age >18 years); 2) patients who were diagnosed with IgAN on renal biopsy; and 3) Beck Depression Inventory-II (BDI-II) score >14. Exclusion criteria were 1) patients awaiting kidney transplantation or those who have already undergone kidney transplantation; 2) patients with multiple organ diseases such as heart dysfunction, chronic

rheumatic diseases, or liver dysfunction; and 3) patients who refused to participate in the study. Our study was approved by the Ethics Committee of Ningbo Urology and Nephrology Hospital (Protocol No. GI-R-01-2011), and written informed consent was obtained from each patient.

Physical activity program

The included patients were randomly divided into a PA group and a control group. We developed a 6-month personalized PA training program for each patient in the PA group. Patients in the control group received treatment as usual. Before the start of PA, we assessed exercise risks in each patient, to develop an individualized PA training program for each participant. Training generally included 30 minutes of cycling exercise (graded exercise treadmill) and 30 minutes of flexibility exercises (limb and abdominal muscle strength). The initial exercise time was 3 times a week for 60 to 80 minutes per session; this was gradually increased to the maximum exercise tolerance, according to each patient's condition. The maximum exercise duration was no longer than 120 minutes. The exercise training process was carried out under the supervision of two physicians and three rehabilitation instructors specialized in sports physiology. The data were recorded by a professional rehabilitation engineer. At enrollment and after 6 months of PA training, depression levels in each patient were scored by a psychiatrist.

At the beginning and after completion of the training intervention, we conducted a spiroergometric study to assess participants' cardiopulmonary function. We recorded exercise indicators such as maximum heart rate (HR_{max}), maximum systolic blood pressure, maximum diastolic blood pressure (dBP_{max}), physical activity time (PAT), maximum pulmonary ventilation (PVE_{max}), peak aerobic capacity (VO_{2peak}), and metabolic equivalents (METs). PA training was stopped if the patient reached their target heart rate or experienced any of the following: arrhythmia, hypotension, hypertension, difficulty breathing, dizziness, or ST segment shift >2.0 mm on electrocardiography. Patients who experienced acute myocardial infarction or severe acute heart failure (New York Heart Association class 4) during training would be withdrawn from the study; however, there were no such events during our study. PA training for patients undergoing regular hemodialysis was performed on a non-dialysis day. During the study, participants were required to maintain a stable diet and level of alcohol consumption, dialysis schedule, and medication regimen. Patients were asked not to use antidepressants or other psychotropic medications. In addition, we recorded the number of hemodialysis sessions required by each patient per month.

Related questionnaires

Prior to the beginning and at the end of the PA training intervention, all participating patients were asked to complete the following questionnaires. 1) The Beck Depression Inventory-II (BDI-II) contains 21 questions, each with a score of 0 to 3. The criteria for depression are as follows: scores of 0 to 13 indicate no depression, 14 to 19 indicate mild depression, 20 to 28 indicate moderate depression, and scores of 29 to 63 indicate severe depression.[11] 2) The Eysenck Personality Questionnaire (EPQ) is based on factor analysis summarizing three orthogonal dimensions and proposing three basic factors that determine personality: internal and external (E), neuroticism (also known as emotional stability or instability) (N), and psychoticism (which refers to psychological or mental qualities) (P).[12] 3) The Quality of Life Index (QLI) consists of five indicators: patient's health, support, daily living, activity, and outlook.[13]

4) The Life Satisfaction Index (LSI) is a self-administered questionnaire comprising 12 items, such as family support, friend support, sexual life, physical and mental health, and hobbies, among others.[14] 5) The Short Form-36 (SF-36) questionnaire is a health survey with 36 questions and includes a Physical Component Scale (PCS) and Mental Component Scale (MCS).[15]

All patients were followed for 1 year, at which time the overall condition of the patients was reassessed.

Statistical analysis

We present categorical variables as number (interquartile range) and continuous variables as median ± standard deviation. We used parametric tests to rule out potential errors in non-normal distributions of the data. We performed the Shapiro–Wilk test of normality for the remaining data; the results indicated that the data followed a normal distribution. We used Pearson's χ^2 test to compare categorical variables and the nonparametric Student *t*-test to compare continuous variables between the PA group and control group. We used a power analysis test to ensure that the study included a sufficient number of participants and that the conclusions were unbiased. Furthermore, we calculated multivariate logistic regression models to confirm the risk factors affecting QLI. SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) was used to analyze all data, and $P < 0.05$ was set to indicate statistical significance.

Results

Characteristics of patients with IgAN

A total of 1658 patients were screened for eligibility in our study, among which 726 (43.8%) were diagnosed with IgAN on renal biopsy. The average participant age was 55.8 ± 12.6 years; there were 736 male and 922 female patients. A total 216 patients with IgAN (29.7%) were determined to have depression and were randomly divided into the PA group (n = 108) and control group (n = 108). At enrollment, there was no significant difference between the two groups with regard to age, sex, renal function, and pathological stage (Table 1). There was also no significant difference between the groups in terms of smoking, drinking, hypertension, diabetes mellitus, myocardial injury, coronary heart disease, pulmonary dysfunction, stroke, and hemodialysis (Table 1). During the study, there were no severe complications associated with PA, such as cardiovascular, musculoskeletal, or other complications.

Physical activity (PA) improves depression symptoms in patients with IgAN

At patient enrollment, there was no significant difference between the two groups in terms of cardiopulmonary function (spiroergometric data), depression levels (BDI-II), personality traits (EPQ), and scores for health-related quality of life (HRQL), as assessed using the QLI, LSI, and SF-36 (Table 2). However, after the training intervention, cardiopulmonary function was significantly improved in the PA versus the control group: $HR_{resting}$ (72.6 ± 7.5 vs. 82.1 ± 9.8, $P < 0.001$), HR_{max} (138.8 ± 17.1 vs. 149.6 ± 18.4, $P < 0.001$), $sBP_{resting}$ (132.3 ± 10.9 vs. 145.8 ± 14.9, $P < 0.001$), and $dBP_{resting}$ (76.5 ± 6.9 vs. 91.2 ± 4.9, $P < 0.001$) were significantly decreased; METs (12.4 ± 2.6 vs. 11.2 ± 1.5, $P < 0.001$), PVE_{max} (60.1 ± 15.6 vs. 37.3 ± 14.1, $P < 0.001$), and VO_{2peak} (27.7 ± 6.1 vs. 20.2 ± 4.1, $P < 0.001$) were significantly increased. Depression levels and HRQL were significantly improved among patients in the PA group as compared with controls; scores on the BDI-II ($P < 0.001$) and EPQ ($P < 0.001$) were significantly decreased, and scores for the QLI (9.6 ± 1.5 vs.

Table 1. Characteristics of patients with IgAN and depression symptoms at enrollment.

	PA group (n = 108)	Control group (n = 108)	*P* value
Demographic characteristics			
Age (years)	56.1 ± 10.8	58.1 ± 9.7	0.15
Female sex (n, %)	67 (62.0%)	63 (58.3%)	0.58
Renal function			
BUN (mmol/L)	56.2 ± 12.1	55.9 ± 13.6	0.86
Scr (μmol/L)	612.4 ± 102.3	631.9 ± 98.6	0.15
eGFR (mL/minute/1.73 m^2)	34.9 ± 10.3	36.2 ± 11.6	0.38
Pathological staging (n, %)			
IgAN I-III	71 (65.7%)	75 (69.4%)	0.56
IgAN IV-V	37 (34.3%)	31 (28.7%)	0.38
Clinical records (n, %)			
Smoking	45 (41.7%)	51 (47.2%)	0.41
Drinking	52 (48.1%)	49 (45.4%)	0.68
Hypertension	71 (65.7%)	69 (63.9%)	0.78
Diabetes mellitus	68 (63.0%)	73 (67.6%)	0.48
Myocardial injury	23 (21.3%)	26 (24.1%)	0.63
Coronary heart disease	23 (21.3%)	27 (25%)	0.52
Pulmonary dysfunction	16 (14.8%)	18 (16.7%)	0.71
Stroke	4 (3.7%)	6 (5.5%)	0.52
Hemodialysis	38 (35.2%)	42 (38.9%)	0.57

Note: Data are median (interquartile range) or number (%).
Abbreviations: IgAN, IgA nephropathy; PA, physical activity; BUN, blood urea nitrogen; Scr, serum creatinine; eGFR, estimated glomerular filtration rate.

8.9 ± 1.8, $P = 0.002$), SF-36 PCS (47.5 ± 8.7 vs. 44.6 ± 7.1, $P = 0.007$), SF-36 MCS (49.6 ± 9.8 vs. 43.7 ± 7.7, $P < 0.001$), and LSI (56.1 ± 9.7 vs. 47.1 ± 8.7, $P = 0.001$) were significantly increased (Table 2).

Physical activity (PA) is independently related to QLI

We used QLI as a dependent variable. Our multiple logistic regression analysis indicated that regular PA (OR 0.271, 95% CI 0.101–0.384, $P < 0.001$); extended hemodialysis interval (OR 0.136, 95% CI 0.043–0.251, $P < 0.001$); decreased scores on the BDI-II (OR 0.451, 95% CI 0.204–0.614, $P < 0.001$), EPQ (OR 0.991, 95% CI 0.984–0.998, $P = 0.007$), and SF-36 MCS (OR 0.267, 95% CI 0.113–0.586, $P = 0.019$); and increased scores on the SF-36 PCS (OR 0.836, 95% CI 0.712–0.983, $P = 0.030$) were independently associated with improved QLI (Table 3).

Participant follow-up

At the 1-year follow-up assessment, we found that 85% of patients continued to engage in regular PA, according to the requirements after 6 months of PA training. A total of 98% of participants reported that they were satisfied with our program.

Discussion

Physical inactivity is a high risk factor for non-communicable diseases and is associated with decreased quality of life and increased morbidity.[16] According to statistics, about 30% to 40% of the world's population does not meet weekly levels of

Table 2. Comparison of variables between the PA and control groups in patients with IgAN.

	Enrollment			After completing training program		
	PA group (n=108)	Control group (n=108)	*P* value	PA group (n=108)	Control group (n=108)	*P* value
Spiroergometric study						
$HR_{resting}$ (beats/minute)	78.1 ± 9.7	80.1 ± 8.7	0.11	72.6 ± 7.5	82.1 ± 9.8	<0.001
$sBP_{resting}$ (mmHg)	145.2 ± 15.2	142.8 ± 12.3	0.18	132.3 ± 10.9	145.8 ± 14.9	<0.001
$dBP_{resting}$ (mmHg)	89.8 ± 7.3	90.4 ± 5.1	0.48	76.5 ± 6.9	91.2 ± 4.9	<0.001
PAT (minute)	32.5 ± 12.3	31.6 ± 14.7	0.67	73.2 ± 12.7	31.1 ± 15.2	<0.001
METs	10.4 ± 1.8	10.7 ± 1.6	0.20	12.4 ± 2.6	11.2 ± 1.5	<0.001
HR_{max} (beats/minute)	140.1 ± 20.1	140.5 ± 18.9	0.88	138.8 ± 17.1	149.6 ± 18.4	<0.001
sBP_{max} (mmHg)	197.3 ± 18.6	193.1 ± 16.4	0.08	179.1 ± 20.7	180.0 ± 18.5	0.74
dBP_{max} (mmHg)	89.6 ± 8.1	89.3 ± 6.8	0.77	80.1 ± 9.7	82.1 ± 7.8	0.09
Double product	25.3 ± 5.6	26.1 ± 4.5	0.25	21.6 ± 5.1	27.1 ± 4.1	<0.001
PVE_{max} (L/minute)	40.3 ± 11.6	39.6 ± 11.9	0.44	60.1 ± 15.6	37.3 ± 14.1	<0.001
VO_{2peak} (mL/kg/minute)	19.4 ± 5.9	20.1 ± 4.6	0.33	27.7 ± 6.1	20.2 ± 4.1	<0.001
BDI-II scores						
Mildly depressed	16.6 ± 2.1	16.4 ± 1.9	0.46	14.1 ± 1.2	16.3 ± 1.7	<0.001
Moderately depressed	25.2 ± 2.6	24.9 ± 2.3	0.37	21.0 ± 1.6	25.1 ± 2.5	<0.001
Severely depressed	48.2 ± 11.3	49.1 ± 9.8	0.53	33.4 ± 9.6	46.1 ± 10.1	<0.001
EPQ scores						
Psychoticism	7.2 ± 1.6	6.9 ± 1.5	0.16	5.6 ± 0.8	7.2 ± 0.9	<0.001
Neuroticism	12.1 ± 2.4	12.3 ± 1.9	0.50	9.1 ± 1.8	11.9 ± 1.2	<0.001
Extroversion	9.8 ± 1.7	10.1 ± 1.6	0.18	7.8 ± 1.5	9.7 ± 0.9	<0.001
Lies	11.7 ± 1.3	11.5 ± 1.2	0.24	8.2 ± 1.0	11.7 ± 1.2	<0.001
HRQL scores						
QLI	7.2 ± 1.6	7.3 ± 1.8	0.67	9.6 ± 1.5	8.9 ± 1.8	0.002
SF-36 PCS	41.6 ± 7.2	39.9 ± 6.8	0.08	47.5 ± 8.7	44.6 ± 7.1	0.007
SF-36 MCS	45.1 ± 9.1	44.7 ± 7.9	0.73	49.6 ± 9.8	43.7 ± 7.7	<0.001
LSI	40.6 ± 8.5	41.1 ± 9.7	0.69	56.1 ± 9.7	47.1 ± 8.7	0.001

Note: Values are median ± standard deviation.

Abbreviations: IgAN, IgA nephropathy; PA, physical activity; HR, heart rate; sBP, systolic blood pressure; dBP, diastolic blood pressure; PAT, physical activity time; METs, metabolic equivalents; PVE_{max}, maximum pulmonary ventilation; VO_{2peak}, peak oxygen uptake; BDI-II, Beck Depression Inventory-II; EPQ, Eysenck Personality Questionnaire; HRQL, health-related quality of life; QLI, Quality of Life Index; SF-36 PCS, Short Form-36 Physical Component Scale; SF-36 MCS, SF-36 Mental Component Scale; LSI, Life Satisfaction Index.

physical activity, as recommended by the World Health Organization, and more than 10% of individuals who are physically inactive die as a result of non-communicable diseases each year.[17] Patients with CKD have reduced exercise tolerance, decreased cardiopulmonary function, and slow metabolism, so they generally have lower levels of PA than the general population.[18,19] Over time, catabolic adaptation in patients with CKD can lead to limited musculoskeletal function, an increased incidence of inflammation in the body, and increased malnutrition, which in turn can further affect patients' quality of life and mental health.[20]

In this study, we collected detailed clinical data of patients with IgAN.

Table 3. Multivariate logistic regression analysis of risk factors related to quality of life index.

	Adjusted OR	Adjusted 95% CI	*P* value
Age (years)	0.621	0.143–3.967	0.607
Female sex	0.827	0.618–1.108	0.515
Physical activity	0.271	0.101–0.384	<0.001
Hemodialysis	0.136	0.043–0.251	<0.001
BDI-II score	0.451	0.204–0.614	<0.001
EPQ score	0.991	0.984–0.998	0.007
SF-36 PCS	0.836	0.712–0.983	0.030
SF-36 MCS	0.267	0.113–0.586	0.019
LSI	1.109	0.895–1.201	0.644

Abbreviations: OR, odds ratio; CI, confidence interval; BDI-II, Beck Depression Inventory-II; EPQ, Eysenck Personality Questionnaire; SF-36 PCS, Short Form-36 Physical Component Scale; SF-36 MCS, SF-36 Mental Component Scale; LSI, Life Satisfaction Index.

Targeted physical exercise training was provided for patients with IgAN in the PA group. At enrollment, all patients with IgAN had lower values of spiroergometric data, indicating that these patients had poor cardiopulmonary function. Because patients with IgAN have chronic anemia, skeletal muscle atrophy, and malnutrition, it is difficult for these patients to meet the levels of PA recommended for the general population owing to their low tolerance for activity. In addition, the incidence of cardiopulmonary insufficiency is often substantially higher in this population than in the general population.[21] However, after 6 months of rigorous PA training, cardiopulmonary function indicators in our patients with IgAN were significantly improved. These results suggest that regular PA in patients with IgAN can significantly improve cardiopulmonary function.

At enrollment, 216 patients were found to have depression, accounting for 29.7% of all patients with IgAN. Our data indicated that the incidence of depression in patients with IgAN was high; this proportion can be expected to increase as life pressures increase. Most patients with IgAN (70.4%) had moderately to severe depression, similar to the results of previous studies among patients with CKD.[22] In addition, as a common mental illness, depression is more often investigated in patients undergoing hemodialysis; the reported incidence rate is between 12% and 45%, owing to differences in study methods.[23–25] Over the past half century, many tools have been proposed to assess depression and quality of life. In this study, we used the BDI-II and EPQ to assess depression levels and the QLI, LSI, and SF-36 to assess patient quality of life. Although the assessments and methods used were different to those used in other studies, our results were similar. All patients with IgAN had high levels of depression and low quality of life at enrollment, suggesting that patients with high depression levels had poor quality of life. A study by Lamping et al.[26] found that the psychological scores of people with illness older than age 70 years were similar to those of their younger counterparts because older people are more likely to accept having a disease than younger people.

We used QLI as a dependent variable. Our results showed that regular PA; extended interval between hemodialysis; decreased scores of the BDI-II, EPQ, and SF-36 MCS; and increased SF-36 PCS scores

were independently associated with improved QLI. Regular PA training improved physical fitness (increased by approximately 15%) in our patients with IgAN. The present results were consistent with those of Painter et al.[27] in patients undergoing hemodialysis. In our study, PA resulted in a 35% reduction in the number of patients with IgAN who had moderate to severe depression. The overall levels of depression in patients with IgAN were also significantly reduced. However, Suh et al.[24] showed that depression levels improved in patients undergoing hemodialysis after 12 weeks of physical exercise, although the result was not statistically significant; limited PA training time might be an important reason for the non-significant findings in that study.

We followed patients with IgAN who participated in the PA training and found that after 6 months of physical exercise, 85% of patients continued to engage in regular PA according to the requirements during the training period. After the PA training intervention, patients reporting feeling more confident and that their self-care ability and health had improved considerably. A total of 98% of participants stated that they were satisfied with our PA program.

This study has three limitations. First, all patients included in our study completed a physical exercise program. However, for various reasons such as work, weather, or personal family issues, some patients could not participate in all training sessions. Therefore, the data of these patients might not be accurate. Second, patients with IgAN who began hemodialysis after they had begun the PA training program were not excluded, and the training program was not changed during the study. For this reason, the data obtained might be heterogeneous. Third, the assessment of depression levels and quality of life in our study was somewhat restrictive and the data presented might be subject to error.

In conclusion, regular PA significantly improved cardiopulmonary function, depression symptoms, and health-related quality of life in patients with IgAN. We found that regular PA; an extended hemodialysis interval; decreased scores for the BDI-II, EPQ, and SF-36 MCS; and increased SF-36 PCS scores were independently associated with improved QLI.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This study was supported by Zhejiang Natural Science Fund (LQ18H150001) and Zhejiang Provincial Medical and Health Fund (2020KY815).

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