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Correspondence should be addressed to Paweł Bogdański, E-mail: pawelbogdanski@wp.pl, Tel: 48-502335001.

Biographical note of the first author: Monika Szulińska, born in 1974, female, doctoral degree in medicine, majoring in obesity, hypertension and endothelial function.
INTRODUCTION

The second most important contributor to the relative risk of developing end-stage renal disease (ESRD) after proteinuria is the body mass index (BMI)\(^{[1-2]}\). The cause of renal disease associated with abdominal obesity is not well understood, but two relevant elements emerge. The first is the presence of obesity-related glomerulopathy (ORG) and the second is the deposition of fat in the kidney with an impact on renal hemodynamics and intrarenal regulation. The exact mechanisms that link abdominal obesity and renal damage are complex and include hemodynamic changes, inflammation, oxidative stress, apoptosis, and finally renal scarring\(^{[3-4]}\).

The prevalence of ESRD in a group of people with BMIs between 18 and 24.5 kg/m\(^2\) is approximately 10 per 100,000; for BMIs >40 kg/m\(^2\), it increases to 108 per 100,000, independently of blood pressure or the coexistence of diabetes mellitus. ORG is observed in abdominally obese people, and particularly in individuals with a BMI >40 kg/m\(^2\). In addition to abdominal obesity, ORG patients present proteinuria without swelling, normalalbuminemia, and focal segmental glomerulosclerosis without nephrotic syndrome\(^{[5]}\). It has been documented that microalbuminuria and elevated albumin-to-creatinine ratios (ACR) are independent factors for cardiovascular risk and cardiovascular mortality\(^{[6-7]}\). Moreover, the risk of developing microalbuminuria is higher in patients with metabolic syndrome\(^{[8]}\).

To avoid kidney damage in subjects with abdominal obesity, a combination of weight reduction and waist circumference reduction with the proper control of renal parameters and obesity-related cardiometabolic risk factors, including metabolic syndrome components such as hypertension, diabetes, and dyslipidemia is required. The standard therapy for abdominal obesity is based on improving physical activity and diet. It has been also observed that physical activity may have a nephroprotective effect that is not dependent on the decrease in body mass\(^{[9-10]}\). Currently, the optimal model of physical training in the treatment of abdominal obesity is being discussed. There is scientific evidence for the superiority of mixed endurance-strength training over endurance training alone in terms of the improvement it produces in parameters such as waist circumference\(^{[11]}\), total body fat percentage, total body lean mass, total body fat-free mass\(^{[12]}\), resting diastolic blood pressure, resting systolic blood pressure, and resting heart rate\(^{[13]}\). However, to the best of our knowledge, there is no strong evidence of the superiority of any type of physical training in the treatment of obesity-related abnormalities of kidney function. The aim of this study was to compare the effect of endurance training with that of endurance-strength training on renal function in abdominally obese women with renal hyperfiltration.

METHODS

Study Patients

There were 163 registered women with obesity screened at the outpatient clinic of the Department of Internal Medicine, Metabolic Disorders, and Hypertension, University of Medical Sciences, in Poznań, Poland. Among them, a total of 44 women were enrolled.

The inclusion criteria were subjects who provided written and informed consent; age 18 to 65 years; simple obesity (BMI ≥30 kg/m\(^2\)); waist circumference >80 cm; content of body fat assessed by electrical bioimpedance ≥33%; and stable body weight in the month prior to the trial (the permissible deviation was ±1 kg).

The exclusion criteria were subjects with diabetes mellitus; a secondary form of obesity (obesity resulting from any underlying disease) or a secondary form of hypertension (hypertension resulting from any underlying disease); poorly controlled hypertension (mean systolic blood pressure >140 mmHg and/or mean diastolic blood pressure >90 mmHg) during the month prior to the trial or the necessity to modify antihypertensive treatment in the 3 months prior to the trial; a history of coronal artery disease; stroke; congestive heart failure; clinically significant arrhythmias; malignancy; a history of the use of any dietary supplements in the 3 months before the study; lipid disorders requiring drug treatment in the 3 months prior to the trial or during the trial; abnormal thyroid gland function; serious liver or kidney dysfunction; clinically significant acute or chronic inflammatory process within the respiratory, digestive, or genitourinary tract, or in the oral cavity, pharynx, or paranasal sinuses, or connective tissue disease or arthritis; history of infection in the month prior to the study; nicotine, alcohol, or drug abuse; pregnancy, childbirth, or lactation at enrollment or
in the 3 months prior to enrollment; or any other condition that, in the opinion of the investigators, would make participation not in the best interest of the subject, or could prevent, limit, or confound the efficacy (not allow to receive an objective result) of the study. The occurrence of any of the above exclusion criteria during the trial resulted in immediate cessation of participation in the study. The characteristics of the study groups are presented in Table 1.

Informed consent in writing was obtained from all subjects. The study protocol was approved by the Ethics Committee of Poznań University of Medical Sciences (registered as case No. 1077/12 with supplement No. 753/13). The present study was performed in accordance with the standards of the Declaration of Helsinki in its revised version of 1975 and its amendments of 1983, 1989, and 1996.

**Study Design**

The study was designed as a prospective randomized trial. Subjects were randomized into two groups, group A and group B, using a randomization list. Each subject had a unique blinded code, and the randomization was performed using the list of codes. Both groups performed 3 months of physical training. Group A underwent endurance training alone while Group B underwent endurance-strength training of comparable exercise volume. Aside from the training, all subjects were instructed to maintain their usual physical activity and diet. At baseline and after 3 months of physical training, blood and urine samples for laboratory analyses were taken, and anthropometric measurements were performed in both groups.

**Anthropometric Measurements**

Anthropometric measurements were conducted with the subjects wearing light clothing and no shoes.

**Table 1. Characteristics of the Study Groups before the Intervention**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Intervention</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
</tr>
<tr>
<td></td>
<td>(n=21)</td>
<td>(n=17)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.3±8.3</td>
<td>48.2±11.2</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>91.7±11.8</td>
<td>94.5±13.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>35.2±3.9</td>
<td>34.9±3.8</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>110.8±10.2</td>
<td>111.6±11.3</td>
</tr>
</tbody>
</table>

**Note.** Results are given as means±SDs. BMI: body mass index; NS: nonsignificant.

Weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. The BMI was calculated as weight divided by height squared (kg/m²). Obesity was defined as a BMI ≥30 kg/m². Waist circumference (cm) was measured to the nearest 0.5 cm at the level of the iliac crest at the end of normal expiration. According to European guidelines, in women, a waist circumference of 80 cm or higher is categorized as abdominal obesity.

**Laboratory Analysis**

Parameters specific to kidney function are blood creatinine level, urine creatinine level, and urine albumin level. The urine creatinine level and urine albumin level were used to calculate the ACR as the urine albumin level (mg) divided by urine creatinine level (mmol). The ACR is a good indicator of early kidney damage. The blood creatinine level was used to calculate the glomerular filtration rate (GFR). The GFR was calculated from the modification of diet in renal disease formula (GFR-MDRD) and the Cockcroft-Gault formula (GFR-CG). Blood creatinine and urine creatinine levels were measured with the Jaffe reaction. The urine albumin level was measured by immunoturbidimetry. Absorption spectrophotometry was used (ADVIA® 1800, Siemens, Berlin, Germany). The accuracy and precision of the technique used to assay these parameters were validated. Reproducibility was checked with a control of human serum and urine (Alab Laboratory®, Poznań, Poland). Measurements were performed using commercial kits (Siemens Healthcare Diagnostics Inc.®, Erlangen, Germany).

**Dietary and Supplement Intake**

At baseline, every 14 days during the intervention, and upon completion of the trial, dietary intake was determined on the basis of dietary intake interviews. A modified food frequency questionnaire was used. The level of nutrients in the daily diet was evaluated using a dietetics computer program. The intake of nutrients, the total caloric intake, and caffeine consumption during the study were constant and comparable between the groups. Subjects were instructed not to use any dietary supplements.

**Intervention**

The 3-month intervention consisted of a physical exercise program of three sessions per week. The women in each group participated in a total of 36
Effects of exercise on renal function in obesity

training sessions over a period of 3 months. During each session, the exercise was performed in a professional training room under the supervision of a certified fitness instructor and a physician. The women in group A underwent endurance exercise on cycle ergometers (Schwinn Evolution, Schwinn Bicycle Company®, Boulder, Colorado, USA). The exercise sessions consisted of a 5-min warm-up (stretching exercise) at low intensity (50%-60% of maximum heart rate), a 45- min exercise session (at 50%-80% of maximum heart rate), 5 min of cycling without a load, and 5 min of closing stretching and breathing low-intensity exercise. Group B underwent endurance-strength exercise, which consisted of a 5- min warm-up (stretching exercises) of low intensity (50%-60% of maximum heart rate), a strength component, an endurance component, cycling without a load, and a closing exercise. The strength component involved a 20- min strength exercise with a neck barbell and a gymnastic ball. Immediately after the strength exercise, the women performed a 25- min endurance exercise on cycle ergometers (Schwinn Evolution, Schwinn Bicycle Company®, Boulder, Colorado, USA) at 50%-80% of maximum heart rate, 5 min of cycling without a load, and 5 min of closing stretching and breathing low-intensity exercise. The heart rate during the training was monitored using Suunto Fitness Solution® devices. Both training programs were comparable in exercise volume and varied only in the nature of the effort. A detailed training program is described in our previous paper[14]. Both exercise programs improve cardiorespiratory fitness[13].

Statistical Analysis

Data are presented as mean±standard deviations (SDs). All calculations and statistics were performed using STATISTICA 10.0 software (StatSoft®, Inc. 1984-2011, Poland). Comparisons between groups were performed using the Mann-Whitney U-test. Wilcoxon’s test was used to analyze the statistical significance between variables before and after the 3-month intervention. A P-value of less than 0.05 was regarded as significant. It was calculated that a sample size of at least 16 subjects in each group would yield at least 80% power of detecting an intervention effect that was statistically significant at the 0.05 α level.

RESULTS

In total, 163 subjects were examined during the prerandomization process. Among them, 119 were excluded from the trial for the following reasons: poorly controlled hypertension (49 subjects), history of coronary artery disease (18 subjects), stroke (6 subjects), congestive heart failure (16 subjects), clinically significant abnormal liver function (9 subjects), clinically significant abnormal kidney function (6 subjects), and clinically significant inflammatory process within the respiratory tract (15 subjects). After screening, the remaining 44 subjects were randomized to group A and group B, each consisting of 22 subjects. One subject from group A and five from group B were removed from the trial following randomization because of low attendance during the intervention process (<70%). In total, 38 subjects completed the trial and underwent analysis (21 from group A and 17 from group B). The compliance ratio was 86.4%.

Prior to the intervention, there were no differences in any of the parameters between groups A and B. After the study, for both endurance training and endurance-strength training, similar changes within the variables were observed, and no significant differences between groups A and B were found. The data for study population before and after the intervention are summarized in Table 2.

Significant and comparable decreases in body mass, BMI, and waist circumference in the studied population following the 3-month endurance and endurance-strength training program were reported in our previous study (Table 2)[14]. Both training programs led to a significant increase in blood creatinine (P=0.003 for group A and P=0.021 for group B), which resulted in a significant decrease in the GFR as evaluated by the MDRD formula (P=0.005 for group A and P=0.011 for group B) and in the GFR as calculated by the CG formula (P=0.001 for group A and B). Unlike endurance training alone, endurance-strength training resulted in a significant increase in urine creatinine level and urine albumin concentration (Table 3). Nevertheless, the urine albumin concentration did not exceed the microalbuminuria level. Neither endurance nor endurance-strength training resulted in significant changes to the ACR. A comparison of studied parameters in groups A and B, before and after the intervention, was presented in Table 3.

DISCUSSION

There is little information available on the effect of particular types of physical activity on renal
function in obese women. Our findings show that both endurance and endurance-strength training exert comparable positive effects on renal parameters in women with abdominal obesity. Hyperfiltration, as indicated by the GFR values observed in our studied population at the beginning of the study, was found to return to the normal range after the training program, regardless of the type of exercise. Moreover, our intervention demonstrated that such valuable effects could be achieved in healthy obese women after as little as 3 months of physical activity.

Obesity itself has a significant effect on cardiovascular risk, and also independently affects renal hemodynamics. Obese individuals with a low number of nephrons are likely to be the most susceptible to these changes. As we mentioned previously[14], both types of exercise had a positive effect on the women’s anthropometric parameters, including body mass, BMI, and waist circumference. The decrease in waist circumference is especially significant, as this parameter is an independent factor for cardiovascular risk, according to a number of other studies[19-21]. Multiple mechanisms have been postulated whereby obesity directly affects kidney disease through hyperfiltration, increased glomerular capillary wall tension, and podocyte stress. It has been observed that weight loss reduces the GFR and leads to more effective renal plasma flow and proteinuria[22]. Stern et al. documented that, although 90% of obese Zucker rats die from chronic kidney disease (CKD), this can be prevented with a 20% calorie restriction diet[23]. Chen et al., in a study of 6000 patients, demonstrated that the prevalence of CKD increases with the number of metabolic syndrome components, ranging from 0.9% in individuals with one component to 9.2% in those with five components[24]. Renal hyperperfusion is the

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before Intervention</th>
<th>After Intervention</th>
<th>P-value</th>
<th>Before Intervention</th>
<th>After Intervention</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td>Group A (n=21)</td>
<td>Group B (n=17)</td>
<td></td>
</tr>
<tr>
<td>Blood creatinine (mg/dl)</td>
<td>0.76±0.11</td>
<td>0.73±0.10</td>
<td>NS</td>
<td>0.84±0.11</td>
<td>0.81±0.10</td>
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</tr>
<tr>
<td>GFR-MDRD formula (ml/1.73 m^2·min^-1)</td>
<td>87.8±18.43</td>
<td>93.5±17.87</td>
<td>NS</td>
<td>77.9±12.65</td>
<td>82.5±12.01</td>
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<tr>
<td>GFR-CG formula (ml/1.73 m^2·min^-1)</td>
<td>129.47±33.24</td>
<td>143.91±36.69</td>
<td>NS</td>
<td>114.02±24.98</td>
<td>124.65±26.71</td>
<td>NS</td>
</tr>
<tr>
<td>Urine albumin (mg/L)</td>
<td>5.38±5.71</td>
<td>3.76±1.75</td>
<td>NS</td>
<td>7.00±8.56</td>
<td>6.59±5.95</td>
<td>NS</td>
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<tr>
<td>Urine creatinine (mg/dl)</td>
<td>69.49±31.29</td>
<td>64.87±39.30</td>
<td>NS</td>
<td>91.71±47.51</td>
<td>116.66±69.74</td>
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<tr>
<td>ACR (mg/mmol creatinine)</td>
<td>1.19±2.32</td>
<td>0.76±0.28</td>
<td>NS</td>
<td>1.28±2.42</td>
<td>0.65±0.28</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Note.** Results are given as mean±SDs. GFR: glomerular filtration rate; MDRD: modification of diet in renal disease formula; CG: cockcroft-Gault formula; ACR: albumin/creatinine ratio; NS: nonsignificant.

<table>
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<tr>
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<th>P-value</th>
<th>Group B before Intervention (n=17)</th>
<th>Group B after Intervention (n=17)</th>
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Effects of exercise on renal function in obesity

first stage of CKD and is a significant pathogenic factor of ORG. In our study, we observed relatively high values of GFR, reaching 130 mL/1.73 m²·min⁻¹ in group A and exceeding 130 mL/1.73 m²·min⁻¹ in group B; this indicates the presence of renal hyperperfusion in studied women. Both exercise programs led to significant decreases in the GFR, as calculated from the GFR-MDRD and GFR-CG formulae. Since the former does not adjust for body mass (unlike the latter), it underestimates the GFR in obese people. For this reason, we used the CG formula for people with a BMI >30 kg/m² and additionally confirmed the results. As a consequence of the training, we observed a significant decrease in the GFR-CG to less than 130 mL/1.73 m²·min⁻¹, both after endurance and endurance-strength exercises. These effects are associated with the reduction of hyperperfusion and subsequent ORG risk. Similar results were obtained in the study performed by Bogdański et al. in obese individuals. After 6 months of increased physical activity in patients with simple obesity, these authors observed significant decreases in the GFR-CG, BMI, and waist circumference, and a significant positive correlation between the change in waist circumference and the change in the GFR-CG. Smektała et al., in a study of obese women, also documented significant decreases in the GFR-CG and BMI and a correlation between the BMI and GFR-CG following 3 months of increased physical training combined with a low-calorie diet. Improvements in renal function, in the form of a significant (31%) decrease in proteinuria in patients with nephropathy, were observed in another study after 5 months of low-calorie diet leading to weight reduction. Praga et al. documented an 80% reduction of proteinuria as an effect of 12% body mass reduction in patients with impaired renal function associated with obesity, following 1 year of low-calorie diet.

In our study, we found an increase in urine albumin concentration and urine creatinine level in women following the endurance-strength training, but not the endurance training alone. However, no changes occurred in the ACR in either group. In terms of these parameters, there were also no differences between the studied groups before and after the intervention. Leehey et al. observed a nonsignificant tendency to a decrease in 24-h proteinuria and ACR in seven obese type-2 diabetic patients with CKD following 24 weeks of aerobic training. It has been also found that aerobic exercise decreases microalbuminuria in nondialysis CKD patients. In our study, despite the increase, the urine albumin concentration did not exceed the microalbuminuria range. The increase in the urine albumin and urine creatinine levels following endurance-strength training in our study can be explained by postexercise proteinuria (seen particularly after isometric exercises), increased total body lean mass (seen after endurance-strength training alone), and subsequent increased creatinine synthesis.

Our study is one of the first attempts to evaluate the effect of endurance and endurance-strength training on renal function in obese women, and to identify obesity as an important risk factor in the development of renal failure.

Study Limitations

The major limitation of this study is the relatively small number of study subjects. The main reason for this was the very rigorous inclusion and exclusion criteria. However, these criteria enabled us to select a homogenous group of subjects not encumbered by diseases or states that might have significantly affected the results of the study.

Study Strengths

It is worth emphasizing that the subjects’ compliance ratio was over 85%. Participation in training was also very high, which strongly enhances the credibility of this study. The inclusion and exclusion criteria were very strict, eliminating the effect of disruptive factors, meaning factors that might have affected the objectivity of the study. The greatest strength of the study is its comparative character, which allowed a clear result regarding the superiority of one of the forms of training to be drawn. This approach is not present in any previous study.

Conclusions

Our findings demonstrate strong evidence of favorable and comparable effects of 3 months of endurance and endurance-strength training on renal function in abdominally obese women with renal hyperfiltration. Further studies on a large scale should be considered in order to draw a precise conclusion regarding a clinically relevant, nephroprotective action involving physical activity in obese patients.

DISCLOSURE STATEMENT

The authors indicate no conflicts of interest.
REFERENCES


