Cardiopulmonary functional capacity and the role of exercise in improving maximal oxygen consumption in women with PCOS

Wydolność krążeniowo-oddechowa i wpływ aktywności fizycznej na zwiększenie maksymalnego zużycia tlenu u kobiet z zespołem policystycznych jajników

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Abstract
Polycystic ovary syndrome (PCOS) is one of the most common reproductive disorder in premenopausal women and is frequently accompanied by the presence of cardiovascular risk factors. It has also been recognized that PCOS women are characterized by cardiopulmonary impairment. Reduced cardiopulmonary functional capacity and the autonomic dysfunction associated with abnormal heart rate recovery might be responsible for the increased cardiovascular risk in patients with PCOS. Exercise training has beneficial effects on cardiopulmonary functional capacity and reduces the risk of cardiovascular disease in PCOS women.

Key words: PCOS, cardiopulmonary functional capacity, exercise

Streszczenie
Zespół policystycznych jajników (PCOS, polycystic ovary syndrome) jest jednym z najczęstszych zaburzeń endokrynologicznych u kobiet w wieku reprodukcyjnym. Zespół ten często współwystępuje z czynnikami ryzyka chorób sercowo-naczyniowych. Ponadto wiąże się on z upośledzeniem czynności układu sercowo-naczyniowego oraz dystfunkcja układu autonomicznego, która wiąże się z zaburzeniami normalizacji częstości rytmu serca może być przyczyną zwiększonego ryzyka sercowo-naczyniowego u kobiet z zespołem policystycznych jajników. Ćwiczenia fizyczne mają korzystny wpływ na wydolność krążeniowo-oddechową i powodują zmniejszenie ryzyka sercowo-naczyniowego w tej grupie chorych.

Słowa kluczowe: zespół policystycznych jajników, wydolność krążeniowo-oddechowa, ćwiczenia fizyczne

Introduction
Polycystic ovary syndrome (PCOS) is one of the most common reproductive disorders and affects between 5-10% of premenopausal women [1]. It is characterized by chronic anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovary morphology. PCOS is associated with several metabolic aberrations, of which insulin resistance and hyperinsulinemia are the most significant. Insulin resistance is present in up to 70% of women with PCOS and seems to have a key role in the pathogenesis of hyperandrogenemia and anovulation [2]. Women with PCOS also exhibit obesity, especially with abdominal fat distribution, dyslipidemia, elevated blood pressure, and an increased prevalence of glucose intolerance and type 2 diabetes [2–5]. About 46% of patients with PCOS fulfil the criteria for metabolic syndrome [6]. Recently, low-grade chronic inflammation has been a related complication observed in PCOS. There is evidence indicating increased levels of C-reactive protein, leukocyte numbers, and pro-inflammatory cytokines such as IL-6, IL-18, and TNF-α in PCOS [7]. Altered vascular and endothelial function in women with PCOS is well documented [8]. Insulin resistance together with other metabolic abnormalities, elevated markers of chronic inflammation, and endothelial dysfunction suggest that PCOS women are at increased risk of cardiovascular disease although not all studies are consistent with this.

Cardiopulmonary functional capacity
Cardiopulmonary functional capacity assessed using a cardiopulmonary exercise test and defined mainly by maximal oxygen consumption (VO2_max) is considered a determinant of cardiovascular disease. There is evidence that increased VO2_max is associated with decreased cardiovascular mortality [9]. Orio et al. were the
first, in 2006, assessed cardiopulmonary capacity in young overweight PCOS women [10]. They demonstrated significantly reduced VO2_{max} oxygen consumption at the anaerobic threshold (VO2_{an}), and maximal workload at peak exercise in PCOS patients compared with healthy women. VO2_{max} correlated with homeostasis model assessment (HOMA), glucose-to-insulin ratio, and the area under the curve for insulin (AUC_{ins}) in PCOS subjects. The authors concluded that women with PCOS are characterized by cardiopulmonary impairment with reduced cardiopulmonary functional capacity that may increase the risk of cardiovascular disease. They also hypothesized that insulin resistance is the key pathophysiological mechanism for the reduced functional capacity, probably due to its influence on mitochondrial function. Insulin is a regulator of muscle proteins and can stimulate the synthesis of mitochondrial proteins. An impaired capacity of mitochondria in skeletal muscle was observed in patients with type 2 diabetes. Moreover, there is evidence that hyperinsulinaemia is associated with low skeletal muscle strength, which may subsequently worsen ventilatory function [11].

Cosar et al. compared VO2_{max} and the resting metabolic rate in PCOS women with central adiposity and in age- and body mass index (BMI)-matched controls with a different body fat distribution [12]. The authors did not observe differences in VO2_{max} and resting metabolic rate between the two groups, so they concluded that central obesity was not a determinant of decreased exercise capacity in women with PCOS. This suggests that factors other than central adiposity, perhaps insulin resistance, are the cause of reduced functional capacity in PCOS patients.

### Heart rate recovery

Giallauria et al., contrary to the previous study, showed that overweight PCOS women demonstrated impairment in VO2_{max} and VO2_{at} [13]. Moreover, they observed reduced heart rate recovery (HRR) in PCOS patients after maximal cardiopulmonary exercise stress test. Abnormal HRR correlated inversely with BMI and AUC_{ins} and there was a relationship between VO2_{max} and the AUC_{gh}/AUC_{ins} ratio in the PCOS patients. HRR after exercise is a marker of autonomic function. Attenuation of this parameter reflects unbalanced autonomic activity with reduced parasympathetic components. Abnormal HRR is an independent cardiovascular risk factor and is associated with increased cardiac mortality [14]. Previous studies indicated that reduced HRR is associated with elevated fasting glucose levels and diabetes [15, 16]. In those studies the authors suggested that in PCOS women, insulin resistance led not only to reduced cardiopulmonary capacity, but also to autonomic dysfunction, which might be responsible for the increased cardiovascular risk.

Tekin et al. determined heart rate recovery, systolic blood pressure (SBP) response to exercise, and heart rate variability (HRV) in patients with PCOS [17]. They showed lower HRR, higher SBP at peak exercise, delayed recovery of SBP after exercise, and depressed HRV. All four parameters indicate sympathetic hyperactivity, which is associated with cardiovascular disease. An interesting hypothesis is that sympathetic hyperactivity may play a role in the development of polycystic ovaries. High levels of norepinephrine were observed in rats with induced polycystic ovaries. In women with PCOS, polycystic ovaries have more catecholaminergic nerve fibres than normal ovaries. Furthermore, autonomic dysfunction may influence inappropriate gonadotropin secretion and in this way influence the pathogenesis of PCOS.

### The role of exercise

Regular exercise has beneficial effects on reproductive and metabolic functions in women with PCOS. Recently, favourable results of exercise training on cardiopulmonary functional capacity in PCOS patients was also documented. Randeva et al. examined young overweight and obese PCOS women who had taken a six-month exercise program (at least three walks per week, each walk of 20- to 60-minute duration) [18]. The authors observed a significant rise in VO2_{max}, a significant fall in plasma total homocysteine level, and a decrease in waist-to-hip ratio (WHR) after the 6-month program compared with baseline in the training group. There was no significant change in BMI. The increase in VO2_{max} and decrease in homocysteine levels were not explained by changes in BMI or biochemical parameters. Hyperhomocysteinaemia-inducing endothelial dysfunction, leading to impairment of the coagulation system and activation of oxidative stress, is considered an independent cardiovascular risk factor. Higher homocysteine levels were found in PCOS women and were associated with insulin resistance [19, 20]. Regular exercise, by lowering plasma homocysteine levels and increasing VO2_{max}, may reduce the risk of cardiovascular disease in women with PCOS.

Vigorito et al. assessed the effects of a three-month structured exercise training program on cardiopulmonary functional capacity in young overweight women with PCOS [21]. The authors observed a significant improvement in peak oxygen consumption and in maximal workload in the PCOS patients after 3 months of the program. The exercising women with PCOS showed a significant reduction in BMI and CRP levels and im-
provement in insulin sensitivity. This study provided evidence that exercise improves metabolic functions, decreases chronic inflammation, and improves cardiopulmonary functional capacity in women with PCOS. Ori et al. observed similar results of an exercise training program in PCOS women [22]. Patients with PCOS had improvements in BMI, fasting insulin, AUC_{ins}/AUC_{postData}

Conclusions
A cardiopulmonary exercise test allows a complex evaluation of the cardiopulmonary system and metabolic transformation at the cell level. Maximal oxygen consumption is an important predictor of cardiovascular disease. Current data agree that PCOS women have impaired cardiopulmonary functional capacity. Some studies suggest alterations in autonomic neural control of the cardiovascular system in patients with PCOS. Moreover, PCOS is frequently accompanied by the presence of other cardiovascular risk factors, such as obesity, insulin resistance, hyperlipidaemia, elevated markers of low-grade chronic inflammation, endothelial dysfunction [8], increased carotid intima-media thickness [23], and increased coronary calcium [24]. These findings suggest increased cardiovascular mortality in women with PCOS.

An important role in the treatment of PCOS is lifestyle modification, including diet and exercise. Even a small reduction in body weight improves anthropometric indices, reduces ovarian volume and microfollicle number, and can restore ovulatory cycles, allowing spontaneous pregnancy [25]. Exercise has many benefits for health and cardiovascular risk factors: it decreases the levels of proinflammatory markers, increases insulin sensitivity, and improves cardiopulmonary functional capacity in PCOS women. Therefore, it may reduce cardiovascular morbidity and mortality in these women.

References
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