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The effect of cardiovascular rehabilitation on physical strain tolerance – does gender really matter?

Uticaj kardiovaskularne rehabilitacije na toleranciju fizičkog napora – da li je pol zaista bitan?

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Abstract

Background/Aim. Gender as a risk factor for cardiovascular diseases has been the subject of research in numerous studies. All of them warn of shortcomings in the diagnosis and treatment of women with a coronary artery disease. The aim of this study is to determine whether there is a difference in the effects of cardiovascular rehabilitation (CVR) on the tolerance of physical strain related to gender in examinees with the coronary artery disease. M**ethods.** The study involved 684 patients, 506 (74.0%) men and 178 (26.0%) women. All respondents were referred to the CVR program after surviving a heart attack, percutaneous coronary intervention or surgical myocardial revascularization. During a three-week program of CVR, patients were subjected to the dosed and personalized physical training. At the beginning and at the end of rehabilitation, all patients were tested for physical strain. **Results.** The average strain level in men was significantly higher in the second test (t = 4.368; p < 0.001). Also, the duration of the test was significantly longer in the second test (Z = 11.836; p < 0.001). In women, the average strain level was significantly higher (t = 5.352; p < 0.001), and the duration of the test was significantly longer in the second test (Z = 7.471; p < 0.001). **Conclusion.** A three-week program of CVR led to an improvement in the tolerance of physical strain in both men and women. Our research once again proved that women have an equal benefit as men from the implementation of CVR. Nevertheless, women rarely participate in the CVR programs. It is necessary to make additional efforts in order to further educate physicians and other medical staff about the importance of sending women to the CVR program.

Key words:
cardiovascular diseases; risk factors; sex, factor; rehabilitation; exertion, physical; coronary artery disease.

Apstrakt

Uvod/Cilj. Pol, kao faktor rizika od kardiovaskularnih bolesti (KVB), je bio predmet ispitivanja u brojnim studijama. Sve one upozoravaju na nedostatke u dijagnostičkom pristupu i načinu lečenja žena obolelih od koronarne bolesti srca. Cilj ovog rada bio je da se utvrdi da li postoji razlika u efektima kardiovaskularne rehabilitacije (KVR) na toleranciju fizičkog napora u odnosu na pol kod ispitanika sa koronarnom bolešću srca. **Metode.** U ispitivanje je bilo uključeno 684 bolesnika, od toga 506 (74,0%) muškaraca i 178 (26,0%) žena. Svi ispitanici su upućeni na program KVR u Institut za lečenje i rehabilitaciju Niška Banja nakon preživelog srčanog udara, perkutane koronarne intervencije i/ili hirurške revaskularizacije miokarda. Tokom tronedeljnog programa stacinonarne rehabilitacije, bolesnici su bili podvrgnuti doziranom i personalizovanom fizičkom treningu. Na početku i kraju rehabilitacije svim bolesnicima je urađen test fizičkog opterećenja. **Rezultati.** Kod muškaraca prosečan nivo opterećenja je bio značajno veći na drugom testu (t = 4,368; p < 0,001). Trajanje testa je bilo takođe znatno duže na drugom testu (Z = 11,836; p < 0,001). I kod žena prosečan nivo opterećenja je bio značajno veći (t = 5,352; p < 0,001), a trajanje testa značajno duže (Z = 7,471; p < 0,001) na drugom testu. **Zaključak.** Tronedeljni program KVR doveo je do poboljšanja tolerancije fizičkog napora i kod muškaraca i kod žena. Naše istraživanje je još jednom pokazalo da žene imaju podjednaku korist od sprovođenja KVR. I pored toga žene u značajno manjoj meri participiraju u programima KVR. Neophodno je učiniti dodatni napor kako bi se medicinsko osoblje dodatno edukovalo o značaju upućivanja žena na program KVR.

Ključne reči:
kardiovaskularne bolesti; faktori rizika; pol, faktor; rehabilitacija; napor, fizički; koronarna bolest.

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Introduction

Cardiovascular diseases (CVD) are the leading cause of death in the world. According to the latest data from the World Health Organization (WHO), about 17.9 million people die annually of CVD, which is about 31% of the total mortality [1]. The most lethal CVD are the coronary heart disease (CAD) and stroke. Every year, more than seven million people die of CAD and it is the main cause of death and disability in developed countries [2]. Fibrinolytic therapy, coronarography and, in particular, percutaneous coronary intervention (PCI) have led to a decline in the mortality of CAD [3].

Gender as a risk factor for CVD has been the subject of research in numerous studies. It is believed that almost 1/2 of women over the age of 20 and about 1/3 of men suffer from some cardiovascular diseases [4, 5]. The Framingham study has shown that CAD is more common in men, especially in relation to premenopausal women [6]. On the other hand, recent studies warn of shortcomings in the diagnosis and treatment of women with CAD [7]. A large meta-analysis done by Kim et al. [8] indicated a higher incidence of complications and higher early mortality in women after percutaneous coronary intervention or surgical myocardial revascularization.

Cardiovascular rehabilitation (CVR) is of paramount importance in the secondary prevention of cardiovascular events [9, 10]. This relates primarily to those patients who have suffered a heart attack, have had a surgical revascularization of the myocardium and/or PCI. Cardiovascular rehabilitation does not only include a dosed physical activity, but also an adequate patient education, the struggle against modifying risk factors, psychosocial adaptation, and adequate cardioprotective medication therapy [11]. As such, CVR has been shown to have a great effect on the quality and duration of life [12, 13].

The aim of this study was to determine whether there is a difference in the effects of CVR on the tolerance of physical strain related to gender in examinees with ischemic heart disease.

Methods

The study involved 684 patients, 506 (74.0%) men and 178 (26.0%) women. The average age of the subjects was 60.84 ± 9.81 years. All respondents were referred to the CVR program at the Institute for Treatment and Rehabilitation Niška Banja after surviving a heart attack, PCI and/or surgical myocardial revascularization. During a three-week program of CVR, patients were subjected to the dosed and personalized physical training that involved bicycle riding, walking and cardiovascular exercise programs. At the beginning and at the end of rehabilitation, all the patients were tested for physical strain. The tests were done on the treadmill track using the Bruce protocol. Tests were limited by submaximal heart rate (calculated as 85% from 220-age equation); symptoms and signs like chest pain, lack of air, dizziness, etc., complex heart rhythm disorders, and/or electropathological changes on the electrocardiogram. Electropathological changes involved the occurrence of horizontal and/or down-sloping ST depression ≥ 01 mm. Complex heart rhythm disorders included long-term episodes of bigeminy of ventricular premature complex (VPC) (long term meaning at least four consecutive second-to-normal VPC), couplets of VPC, and ventricular tachycardia.

Over six thousand patients were considered to participate in the study but it involved only 684 of them, as we included only those patients who finished the entire three-week rehabilitation program and had at least two tests during their stay at the Institute. Patients who did not finish the entire program and/or did not have two tests during their stay at the Institute were not included in our study.

Data on the ejection fraction of the left ventricle and other echocardiographic parameters were obtained from the accompanying medical documentation of the patients, while the data on risk factors for CVD were taken with a detailed anamnesis and basic clinical examination.

Statistics

Data were analyzed using SPSS software-version 20. Qualitative data were expressed as frequencies and percentages, while quantitative data were presented as mean ± standard deviations (SD). Data distribution was tested using the Kolmogorov-Smirnov test. Normally distributed data were compared by the Student *t*-test, while the Mann-Whitney test, the Wilcoxon signed Ranks test and the Mc Nemar test were used for abnormally distributed data. For the comparison of frequencies, the chi-square test was used. Statistical significance was accepted for $p < 0.05$.

Results

The age structure of patients did not significantly differ between genders (men: 60.6 ± 9.81 versus women: 61.54 ± 9.83, $t = 1.102$, $p = 0.271$). Myocardial infarction (MI) was more common in women than in men ($\chi^2 = 6.283$; $p = 0.012$). Men were more often subjected to coronary artery bypass grafting (CABG) ($\chi^2 = 12{,}100$; $p = 0.001$). On the other hand, there was no difference in the incidence of PCI in relation to the gender (Table 1).

Table 1

Distribution of MI, PCI and CABG among genders

Parameters	Male	Female	χ^2/t	*p*
MI				
no	109 (21.5)	23 (12.9)	6.283	0.012
yes	397 (78.5)	155 (87.1)		
CABG				
no	286 (56.5)	127 (71.3)	12,100	0.001
yes	229 (43.5)	51 (28.7)		
PCI				
no	230 (45.5)	73 (41.0)	1.449	0.485
yes	276 (54.5)	105 (59.0)		
No. of stents	0.88 ± 1.12	0.97 ± 1.14	0.868	0.386

Results are given as mean ± standard deviation or n (%).
MI – myocardial infarction;
CABG – coronary artery bypass grafting;
PCI – percutaneous coronary intervention.

Distribution of smoking status differed significantly by gender ($\chi^2 = 7.871$; $p = 0.020$). A significantly higher number of non-smokers were among women, while among men there were significantly more former smokers. The incidence of other risk factors for CAD (hypertension, hyperlipidemia, diabetes mellitus, heredity) did not differ between the groups (Table 2).

Also, there was no significant difference in the values of the ejection fraction between men and women (men: 49.9 ± 9.3% versus women: 50.9 ± 9.2%; $p = 0.254$). At the beginning of the CVR program, the first exercise stress tests (EST) were performed. The tolerance of strain on the first test between men and women is shown in Table 3. The test lasted longer in men (Z = 2.621; $p = 0.009$) and men achieved a higher level of strain compared to women ($t = 4.758$; $p < 0.001$). There was no significant difference in the double product before the test, double product standing for systolic blood pressure x heart rate. The double product after the test was higher in men (Z = 2.293; $p = 0.022$). The incidence of complex heart rhythm disorders or ST depression did not differ between the genders.

After a three-week rehabilitation, the patients were again subjected to exercise stress test. The results obtained were almost identical to the first test. The average strain level was significantly higher among men ($t = 5.123$; $p < 0.001$), as well as the duration of the test ($t = 2.264$; $p < 0.024$). There was no significant difference in the duration of the test and the double product before the test. The double product after the test was higher in men (Z = 2.549; $p = 0.011$). The incidence of complex arrhythmias or ST depression did not differ between genders (Table 4).

Table 2

Risk factors for coronary artery diseases

Risk factors	Male	Female	χ^2	*p*
HLP				
no	68 (13.4)	16 (9.0)	2.421	0.120
yes	438 (86.6)	162 (91.0)		
DM				
no	396 (78.3)	134 (75.3)	0.670	0.413
yes	110 (21.7)	44 (24.7)		
AH				
no	89 (17.6)	21 (11.8)	3.272	0.070
yes	417 (82.4)	157 (88.2)		
Smoking				
no	228 (45.1)	99 (55.6)		
yes	101 (20.0)	36 (20.2)	7.871	0.020
former	177 (35.0)	43 (24.2)		
Heredity				
no	296 (58.5)	105 (59.0)	0.013	0.909

Results are given as n (%).
HLP – hyperlipidemia; AH – arterial hypertension; DM – diabetes mellitus.

Table 3

The first exercise stress test (EST)

Parameters	Male	Female	$t/Z^*/\chi^2$	*p*
EST level	2.37 ± 0.95	1.97 ± 0.98	4.758	< 0.001
EST duration (min)	5.31 ± 2.63	4.72 ± 2.78	2.621*	0.009
Double product before	9,814.05 ± 3,969.42	10,045.42 ± 2,190.65	1.916*	0.055
Double product after	23,308.71 ± 12,184.88	20,809.19 ± 3,784.94	2.293*	0.022
ST depression	62 (12.3)	17 (9.6)	0.941	0.332
Arrhythmia		5 (2.8)	3.180	0.075

Results are given as mean ± standard deviation or n (%).

Table 4

The second exercise stress test (EST)

Parameters	Male	Female	$t/Z^*/\chi^2$	*p*
EST level	2.69 ± 0.94	2.28 ± 0.95	5.123	< 0.001
EST duration (min)	6.23 ± 2.71	5.62 ± 2.85	2.264*	0.024
Double product before	9,641.18 ± 2,235.39	9,813.15 ± 2,002.67	1.916*	0.055
Double product after	21,962.51 ± 3,622.89	21,071.10 ± 3,467.63	2.549*	0.011
ST depression	81 (16.0)	25 (14.0)	0.387	0.534
Arrhythmia	39 (7.7)	10 (5.6)	0.864	0.352

Results are given as mean ± standard deviation or n (%).

At the end of the rehabilitation, we compared the results of the first and the second test in order to determine whether there were differences in the effects of CRV on the tolerance of physical strain in relation to the gender of the patients.

The average strain level in men was significantly higher in the second test ($t = 4.368$; $p < 0.001$). The duration of the test was significantly longer in the second test (Z = 11.836; $p < 0.001$). A double product before the test did not show a significant difference, but the double product after the test was significantly lower in the second test (Z = 2,311; $p = 0.021$). ST depression was more frequent in the second test ($\chi^2 = 5.891$; $p = 0.015$) (Table 5).

In women, the average strain level was significantly higher in the second test ($t = 5.352$; $p < 0.001$). The duration of the test was also significantly longer in the second test (Z = 7.471; $p < 0.001$). A double product before and after the test did not differ significantly. The frequency of ST depression in the second test was significantly higher ($\chi^2 = 6.369$; $p = 0.021$); (Table 6).

Thus, a three-week program of CVR has led to the improvement in the tolerance of physical strain in both men and women. Namely, in both groups of patients, the second test lasted significantly longer than the first one, and the patients achieved a higher level of loading in the second test (Tables 5 and 6).

Tables 7 and 8 show the effect of CVR on physical strain rate tolerance in patients with different types of revascularization. In patients with PCI the average strain level was significantly higher in the second test for both men and women ($t = 8.321$; $p < 0.001$ for men; $t = 4.333$; $p < 0.001$

Table 5

Comparison between the first (EST 1) and the second exercise stress test (EST 2) in men

Parameters	EST 1	EST 2	t/Z*/χ^2	*p*
EST level	2.37 ± 0.95	2.69 ± 0.94	4.368	< 0.001
EST duration (min)	5.31 ± 2.64	6.23 ± 2.72	11.836*	< 0.001
Double product before	9,814.05 ± 3,696.42	9,641.18 ± 2,235.39	0.493*	0.622
Double product after	23,308.71 ± 12,184.88	21,962.51 ± 3,622.89	2.311*	0.021
ST depression	62 (12.3)	81 (16.0)	5.891	0.015
Arrhythmia	32 (6.3)	39 (7.7)	1.029	0.310

Results are given as mean ± standard deviation or n (%).

Table 6

Comparison between the first (EST 1) and the second exercise stress test (EST 2) in women

Parameters	EST 1	EST 2	t/Z*/χ^2	*p*
EST level	1.97 ± 0.98	2.28 ± 0.95	5.352	<0.001
EST duration (min)	4.71 ± 2.78	5.62 ± 2.85	7.471*	<0.001
Double product before	10,045.42 ± 2,190.65	9,813.15 ± 2,002.66	1.266*	0.205
Double product after	20,809.19 ± 3,784.94	21,071.10 ± 3,467.63	0.485*	0.628
ST depression	17 (9.6)	25 (14.0)	6.369	0.021
Arrhythmia	5 (2.8)	10 (5.7)	1.029	0.227

Results are given as mean ± standard deviation or n (%).

Table 7

Comparison between the first (EST 1) and the second exercise test (EST 2) in patients with percutaneous coronary intervention

Parameters	EST 1	EST 2	t/Z*/χ^2	*p*
Male, n = 276				
EST level	2.51 ± 0.98	2.88 ± 0.97	8.231	< 0.001
EST duration (min)	5.56 ± 2.70	6.47 ± 2.75	7.519*	< 0.001
double product before	9,317.40 ± 1,840.18	9,350.82 ± 2,026.95	0.013*	0.989
double product after	23,155.51 ± 16,066.83	22,182.48 ± 3,767.56	1.294*	0.196
ST depression	38 (13.8)	49 (17.8)	69.637	< 0.001
submaximal HR	161 (58.3)	198 (71.7)	87.515	< 0.001
Female, n = 105				
EST level	2.08 ± 1.05	2.40 ± 0.98	4.333	< 0.001
EST duration (min)	4.99 ± 3.07	5.91 ± 2.99	4.068	< 0.001
double product before	9,778.29 ± 1,959.29	9,841.90 ± 1,938.57	0.430*	0.667
double product after	20,719.62 ± 3,641.52	21,261.67 ± 3,391.25	1.375*	0.169
ST depression	10 (9.5)	13 (12.4)	61.383	< 0.001
submaximal HR	56 (53.3)	67 (63.8)	33.726	< 0.001

Results are given as mean ± standard deviation or n (%).
HR – heart rate.

for women). Also, the duration of test in these patients was significantly longer in the second test for both men and women (Z = 17.519; $p < 0.001$ for men; Z = 4.068; $p < 0.001$ for women). Moreover, a significantly higher percentage of patients reached submaximal heart rate during the second exercise test for both genders with PCI ($\chi^2 = 87{,}515$, $p < 0.001$ for men; $\chi^2 = 33.726$; $p < 0.001$ for women) (Table 7).

In patients with CABG the average strain level was significantly higher in the second test for both men and women ($t = 5.406$; $p < 0.001$ for men; $t = 1.926$; $p = 0.060$ for women). Also, the duration of test was significantly longer in the second test for both men and women (Z = 10.025; $p < 0.001$ for men; Z = 2.953; $p = 0.003$ for women). Significantly, a higher percentage of patients reached submaximal heart rate during the second exercise test for both genders with CABG ($\chi^2 = 71.136$; $p < 0.001$ for men; $\chi^2 = 24.874$; $p < 0.001$ for women) (Table 8).

A three-week program of CVR has led to an improvement in the tolerance of physical strain in both men and women regardless of the type of revascularization.

Table 9 shows the distribution of drugs used among men and women. It was found that women were significantly more likely to use clopidogrel ($\chi^2 = 5.713$; $p = 0.007$). The use of other drugs did not differ significantly by gender. The most commonly used drugs in both groups of patients were beta-blockers, acetylsalicylic acid and statins.

Discussion

Cardiovascular rehabilitation is an essential part of the secondary prevention of cardiovascular events in patients with CAD [14]. It has been proven that CVR significantly improves the quality of life, reduces mortality and significantly reduces the possibility of a re-coronary event [15–17]. Also, CVR leads to a better lipid profile, weight loss, blood pressure reduction and reduction of cigarette consumption, anxiety and depression [18–19]. However, less than half of the patients are involved in cardiovascular rehabilitation programs [20, 21]. The reason for such low participation lies in the financial and psychosocial reasons, the lack of motivation and age, and the inadequate education on the benefits of CVR [22, 23]. On the other hand, patients are often not referred to the CVR by an authorized physician [24, 25]. The reason lies in inadequate education and not-well-informed medical staff on the importance of CVR.

Table 8

Comparison between the first (EST 1) and the second exercise test (EST 2) in patients with coronary artery bypass grafting (CABG)

Parameters	EST 1	EST 2	$t/Z^*/\chi^2$	*p*
Male, n = 220				
EST level	2.11 ± 0.84	2.36 ± 0.82	5.406	< 0.001
EST duration (min)	4.93 ± 2.47	5.83 ± 2.48	10.025*	< 0.001
double product before	10,775.00 ± 9,681.32	10,101.95 ± 2,479.19	0.855*	0.393
double product after	21,970.32 ± 11,944.42	21,713.59 ± 3,504.81	2.256*	0.024
ST depression	25 (11.4)	33 (15.0)	93.464	< 0.001
submaximal HR	122 (55.5)	147 (66.8)	72.136	< 0.001
Female, n = 51				
Level	1.76 ± 0.73	1.94 ± 0.79	1.926	0.060
Duration	4.59 ± 2.40	5.33 ± 2.58	2.953*	0.003
Double product before	10,172.06 ± 2,189.75	10,031.18 ± 2,283.83	0.338*	0.753
Double product after	20,075.49 ± 4,187.71	20,237.35 ± 3,835.98	0.174*	0.862
ST depression	4 (7.8)	8 (15.7)	23.330	< 0.001
Submaximal HR	19 (37.3)	28 (54.9)	24.874	< 0.001

Results are given as mean ± standard deviation or n (%).
HR – heart rate.

Table 9

Therapy

Drugs	Male	Female	χ^2	*p*
Beta blockers	484 (95.7)	172 (96.6)	0.320	0.572
ASA	483 (95.5)	172 (96.6)	0.448	0.504
Clopidogrel	163 (32.2)	75 (42.1)	5.713	0.017
Ticagrelor	152 (30.0)	50 (28.1)	0.241	0.624
Statins	477 (94.3)	170 (95.5)	0.394	0.530
Sartans	46 (9.1)	14 (7.9)	0.247	0.619
Ca antagonist	101 (20.0)	39 (21.9)	0.307	0.579
ACE inhibitors	380 (75.1)	146 (82.0)	3.553	0.059
Trimetazidine	98 (19.4)	44 (24.7)	2.292	0.130
Nitrate	45 (8.9)	18 (10.1)	0.234	0.629
Tiazide	52 (10.3)	27 (15.2)	3.053	0.081

Results are given as n (%).
ASA – acetylsalicylic acid; ACE – angiotensin converting enzyme.

Most studies on the CVR emphasized that women participate in CVR programs in a significantly lower percentage than man. The reasons are numerous, looking after family members, transport problems and the existence of comorbidity [26–28]. Also, it should be noted that women were significantly less directed to CVR by physicians [29–32]. This again emphasizes a different attitude of the medical profession towards women in terms of adequate diagnostics, timely therapy and appropriate rehabilitation. Namely, numerous studies that compared the importance of gender differences in relation to the frequency of CVD, timely diagnosis and adequate therapy have come to the conclusion that women are not so rarely subdiagnosed and inadequately treated compared to men [33–35]. Lavie and Milani [36] pointed out the effects that CVR has on the quality of life of women with CAD, while Balady et al. [37] proved that CVR improves the tolerance of physical strain for both men and women. A recent research suggests a significant effect that CVR has on female patients. Thus, Colbret et al. [38] proved that CVR resulted in a significant reduction in mortality in women compared to men. Nevertheless, women participate in CVR programs in a significantly lower percentage than men.

The percentage of men and women who participated in the CVR program during the course of our research speaks in favor of the previous claim. Only 26% of the respondents were female patients. During the involvement of the respondents in the study, it was noticed that female patients, more often than men, left rehabilitation earlier. This points to another problem in the implementation of the rehabilitation program in women, which is a low adherence. Female patients have a significantly less adherence during the implementation of rehabilitation programs than men and have previously abandoned rehabilitation [39]. Women examinees who did not complete the three-week program of CVR at the Institute for Treatment and Rehabilitation Niška Banja were not included in our research.

In our study, as well as in most previous ones, the presence of risk factors for CVD was the same in both genders, which again emphasizes that a cardiovascular disease is no longer a "disease of men" as previously stated [40, 41]. It is known that CVR has a positive impact on the reduction of modifying risk factors. Thus, it was proved that patients after the completion of rehabilitation had a better lipid profile, greater weight loss, better tolerance of physical effort and significantly better psychological profile [42–44]. This again emphasizes the importance of rehabilitation in cardiovascular patients, regardless of the gender.

Comparing the first and the second test, we came to a conclusion that both men and women had better tolerance to physical strain after the completion of rehabilitation. It should be emphasized that female examinees, as well as men, in the outcome test achieved a significantly higher level of strain and that the outcome test was significantly longer than the test at the beginning of the rehabilitation. This again emphasizes the positive impact of CVR on improving the tolerance of physical strain for both men and women. Cardioprotective medication therapy did not differ between male and female gender examinees. The most commonly used drugs were beta-blockers, antithrombotic drugs, and statins. A somewhat more frequent use of clopidogrel among female patients supports previous studies that the new P2Y12 inhibitors are slightly less effective than clopidogrel in women, although this does not have a greater impact on the risk reduction of a new CV event [45].

Conclusion

A three-week program of CVR led to the improvement in the tolerance of physical strain in both men and women. Our research has once again proved that women have an equal benefit from the implementation of the CVR programs. Nevertheless, women rarely participate in the CVR programs. It is necessary to make additional efforts in order to further educate physicians and other medical staff about the importance of sending women to CVR.

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