

# CARDIOVASCULAR RECOVERY PARTICULARITIES IN WOMEN

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**Abstract:** Currently, degenerative cardiovascular diseases are similar in women and men with a delay of 10 years in women, delay caused by the protective effects until menopause. Moreover, at a certain age, cardiovascular diseases are more common in women. Of course, the risk factors, such as hypertension, dyslipidemia, obesity, diabetes play a key role in the evolution and prognosis of cardiovascular disease. Today, however, special attention is also paid to the study of new markers of cardiovascular risk, in the conditions in which the endothelial dysfunction and inflammation play a major part in the pathogenesis of microvascular angina, common in women. Cardiac recovery and secondary prevention represent a group of supervised medical programmes aimed at a faster recovery after a cardiac event, with the objectives of stopping or slowing the progression of the disease, risk reduction or optimization, promoting and maintaining a healthy lifestyle. Comprehensive recovery includes patient evaluation, risk stratification, dietary advice, the aggressive treatment of the risk factors, psycho-social and vocational counselling, recommendations for physical activity and workouts. The structure of the training programme must be adapted to the functional capacity measured by exercise testing; therefore, the intensity and duration of exercises need to be individualized, and the progression should be gradual. Exercises should be structured and conducted on intervals rather in small groups. The groups should also provide women with emotional, social and psychological support; there is an unanimous agreement that the benefits of cardiovascular recovery in women are similar to those in men regardless of their age.

**Cuvinte cheie:** factori de risc, recuperare cardiovasculară, sex feminin, boli cardiovasculare degenerative

**Rezumat:** La ora actuală, bolile cardiovasculare degenerative sunt similare la femei și bărbați cu o întârziere de 10 ani la sexul feminin, întârziere derivată din efectele protectoare până la menopauză. Mai mult, de la o anumită vârstă, bolile cardiovasculare sunt mai frecvente la sexul feminin. Desigur, factorii de risc precum hipertensiunea arterială, dislipidemia, obezitatea, diabetul zaharat joacă un rol primordial în evoluția și prognosticul bolilor cardiovasculare. În prezent însă se acordă o atenție deosebită și studierii noilor markeri ai riscului cardiovascular, acestea în condițiile în care disfuncția endotelială și inflamația joacă un rol primordial în patogeniza anginei microvasculare, frecventă la femei. Recuperarea cardiacă și prevenția secundară reprezintă un grup de programe medicale supravegheate care vizează recuperarea mai rapidă după un eveniment cardiac, având ca obiective oprirea sau încetinirea evoluției bolii, reducerea sau optimizarea riscului, promovarea unui stil de viață sănătos și menținerea sa. Recuperarea comprehensivă cuprinde evaluarea pacientului, stratificarea riscului, sfat dietetic, tratament agresiv al factorilor de risc, consiliere psiho-socială și vocațională, recomandări de activitate fizică și programe de antrenament fizic. Structura programului de antrenament trebuie adaptată capacității funcționale determinate prin testul de efort; de aceea, intensitatea și durata efortului necesită a fi individualizate, iar progresia să se facă treptat. Efortul fizic trebuie să fie structurat mai degrabă pe intervale și desfășurat pe grupuri mici. Grupurile trebuie totodată să ofere femeilor un suport emoțional, social și psihologic, existând un acord unanim asupra faptului că beneficiile recuperării cardiovasculare la femei sunt similare cu cele de la bărbați, indiferent de vârsta acestora.

## INTRODUCTION

Cardiovascular diseases are the first cause of death in women in Europe, about 55% of deaths in women are due to these diseases, especially to coronary heart disease and stroke.(1,2,3) If the incidence of coronary heart disease is significantly lower in women compared to men before the age of 50, it subsequently rises to the level recorded in men.(4) In Europe, there are regional variations in cardiovascular mortality, the highest rates being observed in the Central and Eastern European countries.(5) The reasons that underlie these

differences are the interpopulational differences regarding the classical risk factors (smoking, hypertension, dyslipidemia, diabetes, obesity), and in terms of socio-economic factors, diet (high consumption of saturated fats in Eastern Europe, alcohol consumption, low consumption of fruits and vegetables), mental stress, the prevalence of depression, level of healthcare, genetic factors and environmental conditions.(5) There are also significant gaps between different regions of the world. The analysis of regional variations regarding the mortality by cardiovascular diseases is important for the classification of

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countries in countries with increased or decreased risk.

In our country, there is insufficient data to characterize objectively the situation of women in terms of cardiovascular risk and the existing ones reveal that cardiovascular morbidity and mortality are among the highest in Europe.(6) Thus, according to the data published in early 2012 by AHA - Heart Disease and Stroke 2012 Statistical Update, the first three places in the world in terms of mortality from ischemic heart disease and stroke are occupied by the Russian Federation, Bulgaria and Romania.

In this context, both the European Society of Cardiology and the American Heart Association have launched awareness and intervention campaigns on the cardiovascular pathology in women: "Women at Heart", respectively "Go Red for Women". At the same time, the scientific community decided to develop prevention and treatment guidelines addressed mainly to women, (7) the inclusion of women in growing numbers in clinical trials (the previous studies mainly included male subjects, but it was unclear whether these results can be generalized and applied to women).(2)

### **Risk factors**

Of course, the first question that arises is whether the recovery of cardiovascular disease in women has some features that should be considered in the practical application of the recovery programmes. The answer is yes, but in order to be justified, the particularities of cardiovascular disease in women should be primarily discussed. As it was shown in all studies, the first notable feature is the wrong consideration that women have a low cardiovascular risk, that morbidity and mortality of cardiovascular disease is more reduced than in men, and therefore, attention should be paid to cardiovascular risk factors, cardiovascular diseases, diagnosis and treatment, including recovery. This misconception is derived from the actual finding that women are protected from cardiovascular diseases by specific hormones, but this protection is achieved only up to the menopause and later, with a delay of about 10 years as against men, the development of cardiovascular disease becomes similar. Moreover, at a certain age, cardiovascular diseases tend to predominate in women than in males. There are a number of epidemiological studies showing that actually, the morbidity by coronary heart disease is in the end similar in both genders, and morbidity by stroke is greatly in favour of women, probably related to longer life. As previously mentioned, unfortunately the currently available data are reduced, women are under-represented in trials.(8) The insufficient representation derives from what mentioned above, namely the belief that women have a lower cardiovascular risk and therefore, their importance for trials, especially the drug ones is inferior to that of men. On the other hand, their insufficient participation derives from the reduced availability of women to participate in these trials because women, perhaps, encouraged by the so-called hormonal protection, recognize the risk factors less than men and are less willing to treat them, considering that they do not bring a major threat to the future cardiovascular disease.(9) This is untrue, because cardiovascular risk factors bring about a similar risk in women and men with the delay of about 10 years, as mentioned above. Furthermore, the delayed onset of the cardiovascular diseases is actually reduced through the aggressiveness that the cardiovascular risk factors are developed with, in women. As it is well known, there are potentially modifiable risk factors and not modifiable risk factors or, according to the other most current classifications (2), traditional risk factors and new risk factors, which present many features in women.

Since 2004, guides have shown the importance of recognizing the cardiovascular risk factors in women and the classification of women according to the cardiovascular risk, as

high, intermediate and ideal.(2,10) The increased risk does not only defines the presence of coronary artery disease or the cerebrovascular one, the chronic arterial disease or an aortic aneurysm, a Framingham score > 10%, but also the presence of some equivalents of ischemic cardiopathy, such as diabetes and chronic kidney disease.(7) Women at risk has one or more risk factors for cardiovascular diseases including: smoking, poor diet, obesity (especially, the central one), family history of cardiovascular disease at a young age, hypertension, dyslipidemia. This category also includes women with subclinical cardiovascular disease (such as coronary calcifications), with metabolic syndrome, as well as women with reduced capacity at the effort test or who show abnormal heart rate recovery and more recently, females diagnosed with collagen diseases (autoimmune), history of pre-eclampsia, gestational diabetes or pregnancy-induced hypertension. Women with an ideal status of cardiovascular health condition are those with blood pressure values below 120/80 mmHg, total cholesterol below 200 mg / dl glucose levels below 100 mg / dl (obviously, all these without a specific treatment) body mass index (BMI) below 25 kg / m<sup>2</sup>, non-smokers, develop intense physical activity at least 150 minutes / week or 75 minutes / week of moderate exercise or in combination.(2)

Although a positive trend in terms of the influence of the risk factors (at least in some countries such as Finland) has been recorded until 1997, afterwards, it was found that it was not so obvious and the EUROASPIRE studies (performed in the patients with coronary heart disease) showed even the increase of the prevalence of certain risk factors - overweight increased from 76.8% to 82.7%, obesity from 25% to 38%, central obesity from 42.2% to 54.9%, high blood pressure from 54.6% to 55.2%, diabetes from 28% to 17.4%, while only smoking (20.3% vs. 18.2%) and dyslipidaemia (94.5% vs. 28%) recorded a positive influence (EUROASPIRE III vs EUROASPIRE I).(11) Currently, attention is given to studying the so-called "new markers" of cardiovascular risk, given that cardiovascular risk factors and cardiovascular risk assessment scales lead to an underestimation thereof in women. This happens in the conditions in which the endothelial dysfunction and inflammation play a major part in the pathogenesis of microvascular angina, so common in women.(12) These can be classified into three categories: factors of inflammation, hemostasis, and other factors.

### **Factors of inflammation**

#### **Specific cardiac (high sensitivity) C reactive protein (CRP)**

Women had higher mean values of CRP than men, these differences were more evident at puberty.(13) Higher levels are for sure responsible for the increase in the incidence and prevalence of autoimmune disorders in women (rheumatoid arthritis and systemic lupus erythematosus).(14) The number of cardiovascular risk factors is higher, CRP values are higher.(15) In women without cardiovascular disease, elevated levels of CRP are important predictors for the risk of fatal myocardial infarction and stroke. A prospective study of nearly 30,000 women, initially without cardiovascular disease in postmenopausal, identified, in addition to CRP (with the best predictive value), other three inflammatory markers predictive of cardiovascular events: serum amyloid A, IL-6, sICAM1.(16)

The recommended levels for CRP are below 2 mg / dl.(17) Jupiter study demonstrated that the presence of hs-CRP greater than 2 mg / dl and a LDL-cholesterol <130 mg / dL is associated in women with increased risk of cardiovascular events.(18)

### **Hemostasis factors**

The role of the hemostatic system in the pathogenesis of atherosclerosis is well known and there is evidence regarding

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the cardiovascular risk and the involvement of the fibrinolysis and coagulation mechanisms. It is no longer a novelty the fact that increased fibrinogen levels were associated with an increased risk level for myocardial infarction and stroke (both in the healthy patients and in those with cardiovascular diseases).(19)

**Plasminogen activator inhibitor PAI-1.** Its increased levels are found in the patients (irrespective of gender) with coronary heart disease, with increased risk of myocardial infarction.(19)

### Other factors

**Lipoprotein (a)** is high atherothrombotic, its high levels increase the risk of cardiovascular disease, thus representing an independent risk factor for the cardiovascular disease.(20) There is also evidence that the values of Lp (a) increased with age in women, its increased levels accounting for an independent atherogenic risk factor, both in premenopausal and in postmenopausal period.

**Homocysteine.** Elevated levels of homocysteine have also been involved in the pathophysiology of cardiovascular diseases. Recent studies have shown that there are differences between genders regarding serum homocysteine level, women showing lower levels. Homocysteinemia increases with menopause. Also, some studies have reported a relation between serum homocysteine levels and the presence of coronary artery diseases in women but not in men, thus representing a strong atherogenic factor in women.

**Apolipoprotein E (APOE).** It is a component of lipoproteins involved in the modulation of total cholesterol and LDL-cholesterol. Apolipoprotein E levels are higher in postmenopausal women than those in premenopausal and man.

**Cell adhesion molecules ICAM-1 and VCAM-1** play an important part in the pathogenesis of atherosclerosis, especially by their involvement in leukocytes attraction, phenomenon that initiates and promotes inflammation at wound level. The presence of some elevated levels of adhesion molecules have been identified in a wide range of cardiovascular patients: diabetes, obesity, hypertension and dyslipidemia. There is also a direct connection between the levels of adhesion molecules and the thickness of the carotid intima (which is a risk factor for cardiovascular clinical events). Within the MENOCARD grant "Optimizing the treatment of degenerative cardiovascular diseases in postmenopausal women" performed in the Cardiology Rehabilitation Clinic of Cluj-Napoca, studying the adhesion molecules, it has been found that although the levels of sVCAM-1 are influenced by age and the presence of cardiovascular risk factors, in postmenopausal women it is a useful parameter for assessing the risk of cardiovascular disease.

### Ovarian dysfunction

There are studies that showed that ovarian dysfunction due to estrogen deficiency, hypothalamic dysfunction, and irregular menstruation occurring in premenopausal women are associated with increased risk of coronary atherosclerosis and diverse cardiovascular adverse events.

### Recovery situation in women

Based on the peculiarities of manifestation, evolution and treatment of cardiovascular diseases, there is also a number of features in terms of recovery and secondary prevention in women. Cardiovascular recovery in women is not well enough known, because women are undervalued in clinical trials and research on recovery, accounting for only 4-11% of the participants.(21) Even this finding that participation in physical rehabilitation programmes for women with cardiovascular disease is lower than that of men, in the few studies that are at our disposal, among the patients eligible for recovery, only 22-36% of women are included in such programmes, compared to

41-49% of men.(22) Participation depends on a number of factors. The older age is a factor that significantly reduces the percentage of women participating in physical rehabilitation programmes.(23) The level of education is important, higher the level of education, higher the attendance is. The low socioeconomic status reduces the participation in recovery programmes, the percentage decreasing proportionally with the decrease in annual revenue. Not to forget about the marital status, single women (unmarried, divorced, widowed) participated in a significantly lower number than married women.

It is important to reimburse the costs by the insurance companies because it turned out that, women who have health insurance follow a 8.6 times higher rate of recovery programme than those who are not insured. The ratio is higher than in men, case in which the ratio of the insured and uninsured included in the physical training programmes is of only 2.7. We must not forget that the most common comorbidities in women significantly limit their participation in the physical rehabilitation programmes. Comorbidities have two explanations. The first one and most obvious is the older age of women with cardiovascular disease. On the other hand, osteoporosis, much more common in women also has a negative impact on the participation and physical activity, paradoxically as physical exercises reduce the extent and progression of osteoporosis.

We must also take into account the socio-professional motivation, particularly important in determining compliance to the rehabilitation programmes. Due to the fact that 50-59% of the women included in recovery programmes are over 65 years old, professional motivation is low. In fact, the social role is much diminished at this age.(23) It has been shown that women are motivated especially by the elements the family's future depends on, and primarily by the children's future. A second important finding in the women included in recovery programmes is the higher prevalence of the traditional risk factors. The presence such risk factors in a higher degree urges, on one hand to a comprehensive recovery, in which the training and physical activity should be supplemented with secondary prevention measures or lifestyle change, but sometimes, with drug prevention. On the other hand, it forces to changing the recovery programmes in the sense of decreasing the effort intensity during the training session and extending the number of training sessions, the duration of physical recovery. In the women included in the recovery programmes, not only the cardiovascular risk factors are more common, depression and anxiety, as well lead to a lower self-efficacy of which the results of the recovery and long-term participation in the recovery programmes depend on. Consequently, 30% of women stop attending the training programmes one month after their commencement, and 50% 3 months later.(24)

There are other elements regarding the participation of women in recovery programmes, these deriving from the existing reality that at home, women perform more physical activity than men. Thus, 1 month after an acute heart attack, 75% of women resume their household physical activity compared to only 30% of men.(25) Household work is however not done in a manner which ensures the effect of training, but women think that they make sufficient physical activity as not to attend the recovery programmes; secondary prevention is neglected and therefore, less favourable results are recorded regarding the cardiovascular disease evolution. Among the women participating in recovery programmes, the effectiveness of physical activity and the tolerance to physical activity are lower than in men, a finding that should be taken into account when elaborating concrete recovery programmes in women.

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Finally, another explanation for the low quality of recovery in women is that recovery programmes are not sufficiently flexible and educative for women. Regarding the educational aspect, they fail to convince women of the need to change lifestyle in order to influence the risk factors. Regarding flexibility, these are often rigid, with fixed hours of participation, and women, who are more involved in family life, often sacrifice recovery, including their own interest for the family interests.

### Recovery results in women

If participation in physical rehabilitation programmes of females is scarce regardless of age and form of cardiovascular disease for which recovery is performed, in exchange, the results of recovery in many respects are similar both in men and women. Therefore, effort capacity increases similarly in women and men between 10 and 40%, the maximum percentage being recorded in the women with reduced capacity at the moment of their inclusion in the study.(26) Increasing and maintaining moderately high levels of physical activity can prolong life at any age in females, the maximum benefit being observed in women under 75 years old and in those with significant comorbidities.

The second important component of recovery, its direct effect on the risk factors is less important in women and men. In both genders, lipids are influenced only at borderline significance. For significant influence of lipids level, it is necessary to practice a long-term recovery and physical activity. The same insignificant effect is recorded on weight and body components that remain unchanged as a result of recovery programmes. As long as diet and medication programmes are associated, the body weight can be significantly reduced; continued physical activity playing an important part in maintaining body weight. Low direct results on the risk factors do not mean the absence of beneficial effects in terms of secondary prevention, in the case of recovery programmes completed or extended in an extended phase II. It is found that the women who succeeded to complete these programmes, unfortunately an insufficient percentage, have significant benefits in combating risk factors. Summarizing, we can say that the recovery results in women are good and it is surprising that in this situation, the percentage of women included in recovery programmes remains insufficient.

### Recovery methods

Of course, the question is what recovery means we should choose in order to increase, on one hand attendance and on the other hand, the results of recovery, which in women are increasingly affected by cardiovascular diseases. As a first necessity in the recovery of women with cardiovascular diseases, is to increase the rate of inclusion in the rehabilitation programmes. In order to achieve this first step, without which recovery cannot be performed, motivation is of uttermost importance.(27) It has been already mentioned that motivation, that of the close entourage, the family's, is the most important and proved that the most important motivation for women is the one brought by children, so that the adult children must become allies of the recuperator. Also, regarding addressability, we should not forget about the role of the family physician and cardiologist whom women strictly follows his advice; actually, this treating doctor addiction is recorded in the case of smoking, both in women and in men.

Regarding the recovery programmes themselves, they will be adapted to the functional capacity measured by the pre-recovery effort test. It was shown that, in general, exercise capacity and muscle mass of women are lower, which require the selection of special programmes, even personalized for each patient. These programmes should be stimulating for the

purposes of providing the possibility of increasing the exercise capacity. Therefore, it is recommended that training programmes be, at least in a first phase, shorter, the second phase of the recovery to take place over a longer period of time and not to neglect to include women in phase two of extended recovery that can further ensure a significant and radical change of our patients' lifestyle.

Regarding the concrete manner of performing physical training, recovery heart rate should be similar to that of men, and if muscle tolerability is reduced, a moderate physical training activity will be used first in order to reach an intense effort with a heart rate of 70-85% of the maximum heart rate.(28) Taking into account that women get tired faster, interval training is a solution for females because it provides a much better compliance, providing short periods of muscle rest. Another feature of the recovery methodology in women is the need for a high variety of types of effort. Women get bored faster than men so that the use of a single type of training can lead to a rapid decline in interest and recovery abandonment. Of course, overloading should be avoided, as well as overcome hemodynamic condition, but this is the responsibility of the physical therapist who supervises the female patients' recovery. Taking into account the female characteristics, a permanent encouraging attitude will be adopted even in the abandonment periods of time, targeted not so much towards the physical performance, but especially to the successes in preventing the risk factors. To achieve the objectives, in men especially, it is indicated to add the psycho-social support that is able to increase recovery outcomes in women and to reduce depression and anxiety. Thus, the repeated discussions with the social worker, individually or in group with the psychologist are beneficial.

The number of elements that can positively motivate women decreases in case of old women. In this category, the efforts to capture the interest, to obtain the constant participation in the recovery programmes should be higher. It turned out that in older women, home visits and the close relationship with the staff recovery (man to man discussions) significantly increase not only compliance but the cardiovascular recovery results as well. The question is how long does the recovery takes in women and whether it is different or not than in men. The answer is that, in women as in men, the minimum recovery to obtain some benefits is of four weeks, in which maximum results can be obtained if recovery is in hospital. Home recovery is therefore recommended more than in men, because otherwise women are taken out of their environment, removed from their daily preoccupations and the sense of duty that makes them feel being out of time, and as a result they will not participate in the rehabilitation programmes. Of course, the more this limit is extended by 4-6 weeks, the better the results of recovery are and as it has been already mentioned, the need to include, where possible, all the women in phase II of the extended recovery.(22) Given the so different social role of women, from successful business women, women who play important parts in science, education or politics, up to the majority of the women who still remain housewives, it is important that, through the recovery programmes to allow the return to their everyday life. This requires an approach, a motivation and an individualized recovery programme, that in this form will always be successful.

### Conclusions:

At the end of the discussion about cardiovascular diseases recovery in women, we should recall some useful elements:

- maximizing the participation of women with cardiovascular diseases in recovery programmes is done by decreasing or lowering the barriers that limit their participation;

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- it is important to know and recognize gender differences regarding depression and social support;
- gender differences regarding the coronary risk profiles should be also recognized;
- collaboration with family physicians to treat aggressive risk factors is essential;
- an important element that must be taken into account is the difference between young women and postmenopausal women. If postmenopausal women receive special recovery programmes, generally, young women will be subject to a male-type recovery, of course taking into account the peculiarities of the cardiovascular diseases they suffer from.

Thus, we can conclude that in women, it is necessary to apply some creative recovery programmes that should take into account the following:

- individualized application of the recovery programme for each woman, the use of recovery groups for women only, because otherwise, it could be negatively influenced by the higher physical performance of the men from the same batch,
- a leader of the group of women is needed to encourage their participation in the recovery programmes,
- there is need for a greater use of lower intensity exercises but with a longer duration,
- it is necessary to create support women groups, in which women support each other, discuss their problems and encourage each other during the recovery programmes.

By using all these elements, the number of the recovered women will probably significantly increase, so that the recovery results be comparable with those obtained in males.

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