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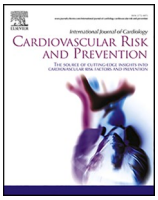

Gender difference in long-term effect of cardiac rehabilitation; data from CRAGE-extra study

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ABSTRACT

Introduction: The positive effect of cardiac rehabilitation (CR) is demonstrated in younger and older patients. However, it is quite debated whether the beneficial effect is similarly maintained in both genders during follow-up.
Aim: to determine if the improvement obtained after CR remained significant at 1-year follow-up in older population, testing the influence of gender on this outcome.
Methods: All patients aged 75+ years consecutively referred to Cardiac Rehabilitation outpatient Unit at Careggi University Hospital were screened for eligibility. All patients attended a CR program, based on 5-day-per-week aerobic training sessions for 4 weeks and they were evaluated at the end of CR at 6 and 12 months of follow-up.
Results: 361 patients with a mean age 80.6 ± 4.4 years with a complete 1-year follow-up were enrolled in the study, 87.5 % of them had an acute coronary event, and 27.6 % were females. The increase in exercise capacity at the end of CR and at 1-year follow-up was statistically significant (VO2 peak: +8.7 % in males $p < 0.001$, +8.5 % in females $p < 0.001$; distance walked at 6-min test: +7.3 % in males $p < 0.001$, +10.2 % in females $p < 0.001$, respectively); the trajectory of exercise improvement at 6 and 12 months of FU was similar in men and women without significant decrease (VO2 peak-ml/kg/min: CR discharge vs 1 year FU = 15.2 vs 15,0 p: NS; distance walked-meters: CR discharge vs 1 year FU = 445.5 vs 440.6, p: NS) from end of CR to 1-year.
Conclusions: the improvement in exercise tolerance obtained with CR program is still maintained at 1-year FU without significant influence of gender in our very old population.

1. Introduction

Cardiac rehabilitation (CR) is recommended by guidelines after cardiac events both in younger and older patients [1]. The beneficial effect of CR is achieved soon after a cardiac event regardless of programs or clinical settings [2]. The rate of older patients enrolled in CR has progressively increased in the last decades. Yet, it remained quite low, with a clear disparity between men and women [3].

The long-term effect of CR is debated and updated in a recent Cochrane Review [2]. The outcome of this research reinforces the benefits of exercise-based CR in cardiac heart diseases, highlighting the reduction of all cardiovascular outcomes. Unfortunately, no data about the effect of CR on global functional capacity or disability level and their trajectories over time are reported as stated by the Authors [2]. In addition, evident sex-specific disparities in referral and participation rates of females are clearly certified despite CR has been shown to reach similar or greater benefits in females compared with males [3]. Thus, we aim to verify if the increase in exercise capacity obtained during CR program in older patients is maintained at the 12-month follow-up, and whether this improvement could be influenced by gender.

2. Methods

The CR-AGE EXTRA's (Cardiac Rehabilitation in Advanced aGE: EXercise TRaining and Active follow-up randomized study) protocol for the CR program, including the details of the exclusion criteria and the

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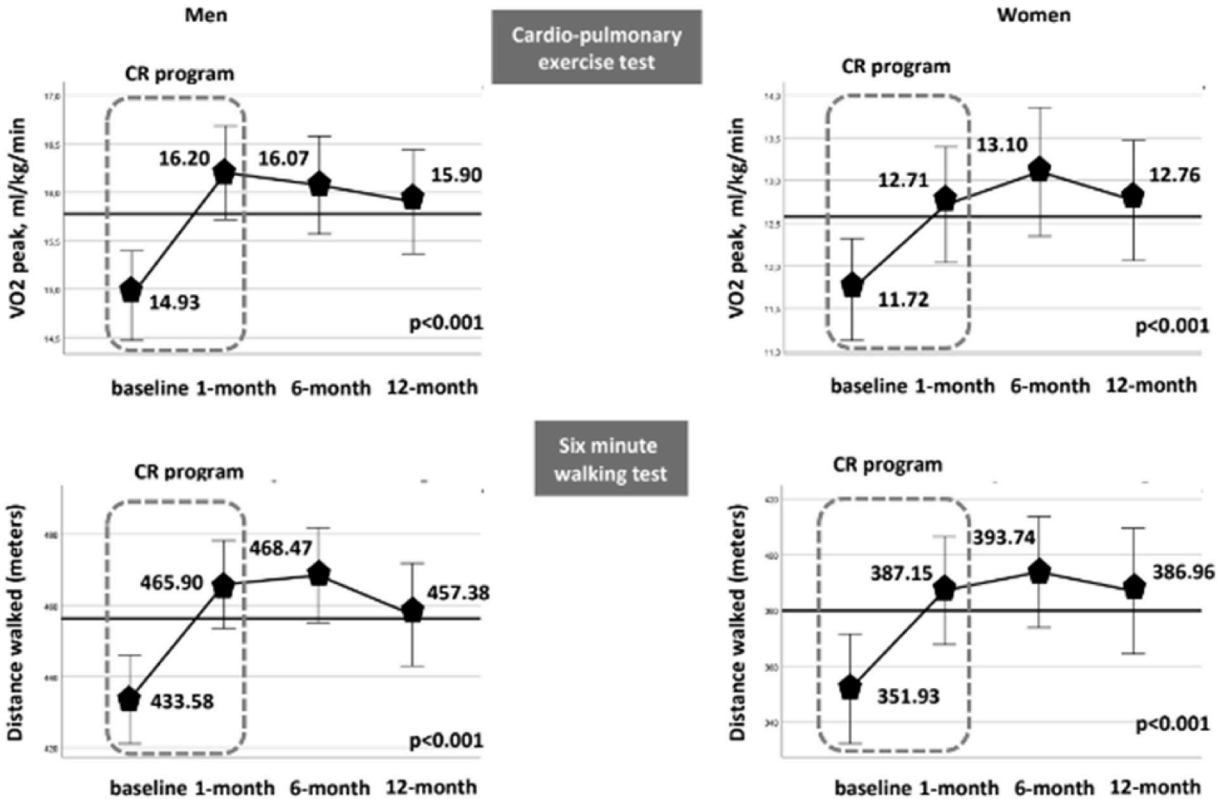

Fig. 1. Temporal trends of performance measures (VO2 peak and distance walked at 6MWT) during CR and 12-month follow-up in both genders.

data collected, has been reported elsewhere [4].

2.1. Study population enrollment and general evaluation

All patients underwent a complete cardiological assessment; in addition, we evaluated patients with a comprehensive geriatric assessment (CGA), measuring their chronic comorbidity burden as well as their ability to perform activity of daily living (ADL sec. Katz) and instrumental activity of daily living (IADL sec. Lawton), cognitive performance and psycho-emotional and socioeconomic profile.

2.2. Functional evaluation

Aerobic capacity was expressed as the maximal oxygen consumption (VO2-peak, ml/kg/min) resulting from breath-to-breath analysis during a symptom-limited cardiopulmonary exercise test (CPET) at cycle ergometer conducted following a 10 Watt/minute incremental workload protocol. Endurance was defined as the total distance walked during a 6-min walk test (6MWT) in a 30-m corridor with telemetric electrocardiogram (ECG) and oxygen saturation monitoring.

2.3. Follow-up program

Starting from the CR discharge visit after 1 month, all patients were scheduled for 6 and 12-month follow-up visits and functional capacity reassessment with CPET and Six-minute walking test.

2.4. Statistical analysis

Statistical analyses were performed using the IBM SPSS v.26 package. Continuous and categorical variables are expressed as mean ± standard deviation or percentages, respectively. Student's t-test and or chi-square test were used for gender-group comparisons of continuous or categorical variables at baseline. General linear models for repeated measurements were tested to compare the time-dependent variance of VO2-peak and distance walked in 6 min during 12-month follow-up visits in the whole study population and in both genders.

The Greenhouse–Geisser correction was adopted when the statistical significance of Mauchly's test for sphericity was violated. A two-sided $P < 0.05$ was considered statistically significant.

3. Results

The main clinical characteristics can be summarized as follows: we enrolled in the study 361 patients with a mean age of 80.6 ± 4.4 years; 87.5 % of them had an acute coronary event, 27.6 % were females, 23.5 % of patients were affected by diabetes, 10.2 % had chronic obstructive pulmonary disease (COPD), 48.8 % presented dyslipidemia; the mean level of hemoglobin was 12.5 ± 1.6 gr/dl, estimated glomerular filtration rate (eGFR) was 62.8 ± 17.5 cc/min. The prescription rate of recommended therapies for coronary artery disease was over 80 % for ace-inhibitors, beta-blockers, antiplatelets, and statins. Significant differences were found in left ventricle ejection fraction (LVEF), hemoglobin, and prevalence of dyslipidemia between males and females.

The exercise capacity at the end of CR and at the 12-month follow-up was higher and statistically significant compared to the baseline (VO2-peak: +8.7 % in males $p < 0.001$, +8.5 % in females $p < 0.001$; distance walked at 6-min test: +7.3 % in males $p < 0.001$, +10.2 % in females $p < 0.001$, respectively).

As expected, the mean level of distance walked at 6MWT and VO2-peak at CPET were statistically higher in males than females. In the figure (*see below*), we showed the temporal trends of performance measures (VO2-peak and distance walked at 6MWT) during CR and at 12-month follow-up in both genders. Data demonstrated similar trajectories of functional performances over time without significant decrease, for each time evaluation. The mean level of distance walked at 6MWT and the VO2-peak were statistically higher in males than females (Fig. 1).

4. Discussion

The main result of our study is that the improvement in exercise tolerance obtained with the CR program is maintained at 12-month follow-up and the temporal trajectories during the follow-up period are substantially similar without differences related to gender.

This finding can contribute to closing the gap of evidence regarding sex-disparities about an early referral and continuous management of older women in CR as a central part of multidisciplinary secondary prevention after an acute cardiac event. In this respect, one should not forget that females showed more complex coronary artery disease and had lower mortality reduction over time compared with males. In addition, they presented more frequent angina, independently from the extension of coronary atherosclerosis, or myocardial ischemia with a consequent great impact on functional capacity and quality of life [2]. Thus, it is hard to accept that outpatient female candidates to CR programs are less likely to be referred [5] than males considering – as reported in our work – that functional benefit obtained during CR is maintained in the follow-up.

Declaration of generative AI in scientific writing

During the preparation of this article the authors didn't present any content generated by AI tools as their own work.

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Declaration of competing interest

The authors declared they do not have anything to disclose regarding no conflict of interest with respect to this work.

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