

## **Exercise Performance in Post-Surgery Cardiac Rehabilitation in Women and Elderly**

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**Received:** August 19, 2020; **Published:** December 31, 2020

### **Abstract**

**Objective:** We hypothesized that post-cardiac surgery rehabilitation (CR) has different efficacy on physical fitness recovery according to gender and age subgroups.

**Design:** 677 post-cardiac surgery CR patients were analyzed, both at admission and at discharge, for fitness and echocardiographic data.

**Results:** At admission, females walked a lower distance at 6-minute walking test, were more compromised in Barthel scale, had lower VO<sub>2</sub> max ( $p < 0.001$  for all) and a worse perception of effort ( $p = 0.001$ ) compared to male. They similarly improved at discharge in all parameters ( $p < 0.001$ ), except for metres walked ( $p = 0.004$ ). Elderly patients ( $>$  median of 68 years) had lower VO<sub>2</sub> max at admission ( $p < 0.001$ ) and improved similarly to adult patients at discharge ( $p < 0.001$ ), except for metres walked ( $p < 0.001$ ). CR produced increment of EF by 10% in patients with reduced and 3% in those with preserved EF ( $p = 0.0002$ ). Physical fitness and E/E' significantly improved in both EF groups. E/E' was greater in elderly patients at admission ( $p = 0.011$ ) and similarly reduced in both age groups ( $p < 0.001$ ) after CR.

**Conclusion:** CR projects should be personalized not only in terms of modalities, volume and intensity of exercise, but also according to the length of hospital stay, taking into consideration gender and age physical fitness peculiarities.

**Keywords:** *Cardiac Rehabilitation; Secondary Prevention; Exercise Training; Cardiac Surgery; Cardiac Function*

### **Introduction**

Cardiac rehabilitation (CR) is a multidisciplinary systematic approach designed to apply secondary prevention therapies of known benefit, inclusive of medical evaluation, prescriptive exercise, cardiac risk factor modification, education, counselling and behavioural interventions [1-3]. The most evidence-based benefits of CR include an improvement in exercise tolerance and psychological well-being, reduction of symptoms, blood lipid levels, smoking, stress and mortality<sup>1</sup>, recurrent myocardial infarction [4]. Specifically designed CR programs are able to improve patient's quality of life and ability to return to work quickly [5]. Physical fitness demonstrates a consistent, inverse association with mortality, even after adjusting for traditional risk factors burden [6]. Exercise training has beneficial effects for patients after myocardial infarction, producing a decrease in heart rate and blood pressure response for any level of physical activity, with improvement in aerobic capacity that averages 20% [7].

Early data suggest that exercise capacity is lower in women than in men, although both sexes achieve the same improvement in functional capacity with training [8]. Although both genders receive equal benefit from participation in CR exercise training, women are 12% less likely to enter CR programs. Moreover, even when referred, women are less likely to attend CR, although the theoretical greater benefit that they could experience, given their less favourable functional capacity at entry [9]. Elderly patients are typically at higher risk of complications from myocardial infarction and myocardial revascularization procedures, leading to prolonged hospital stay and subsequent deconditioning [2]. Additionally, elderly patients are usually less fit than adult patients before the initial cardiovascular event, with accelerated deconditioning once heart disease is established. A randomized controlled trial showed that CR enhances exercise tolerance in patients of all ages, including those older than 75 years [10]. Beneficial effects of CR programs in the elderly have been reported not only on exercise capacity, but also on mortality, psychological risk factors, inflammation and obesity. Similar to women, despite the fact that old patients have special need for CR, there is a bias and poor referral [11].

In this single-centre retrospective study, we analyzed the patient population referred in post-cardiac surgery hospital CR program in terms of gender and age-related clinical characteristics, fitness level and response to training, with the purpose to compare women with men and elderly with adult physical fitness status at admission and discharge. We hypothesized that female and elderly patients begin CR with more compromised physical fitness and, although improving with CR, they do not reach their counterpart functional status at the end of hospital stay.

## Methods

### Study population

Between January 2014 and December 2017, 815 consecutive patients (589, 72%, men and 226, 28%, women) were referred to our CR Unit: only 83 (10%) were admitted from cardiology ward after heart failure, myocardial infarction or pacemaker implantation, while the majority (n = 732, 90%) was referred after major cardiovascular surgery. Only patients who underwent cardiovascular surgery were selected for retrospective analysis. Inclusion criteria reflected standard requirements of appropriateness for admission in the hospital CR, as previously described [12]. Exclusion criteria for the study were incomplete patient charts, inability to perform any physical exercise, cognitive impairment.

The study was approved by hospital ethical committee and conducted in accordance with Declaration of Helsinki for human rights. All enrolled patients gave written informed consent to participate in the study.

### Methods and data analysis

Our CR program is hospital based, with patients admitted directly from post-cardiac surgery ward,  $6 \pm 2$  days after intervention. CR program is patient-tailored based on individual CR project, includes 120 minutes of daily rehabilitative activities, half individual and half in group, and 50 minutes of daily nursing, cardiological, psychological and nutritional activities.

At admission, all patients underwent initial nursing and evaluation of muscular strength and postural changes. Afterward, all patients performed  $10 \pm 3$  days of training session, with incremental intensity and length of exercise, using either treadmill, cyclette, pedals or manual cycloergometer, targeting heart rate between 60% up to 85% of maximal theoretical [13]. Once clinical stability was reached and ability to perform activities of daily living was restored in compliance with the programmed target, patients were discharged. The length of CR hospital stay is rather short since the ward has to accomplish the need of CR of most post-cardiac surgery patients of the hospital.

Physical performance was evaluated both at admission and at discharge. Particularly, ability in daily activities was assessed by Barthel scale [14]. Patients were instructed to perform 6-minute walking test to evaluate their functional capacity: distance walked was measured in metres, while perceived fatigue was evaluated by Borg scale [15]. Furthermore, based on the 6-minute walking test, data on  $VO_2$  max (mL/Kg/min) were calculated in all patients [16].

Complete transthoracic echocardiogram was performed both at admission and at discharge, by the same investigator, using a new generation ultrasound machine (Philips iE33, Milan). Left ventricular (LV) ejection fraction (EF) was measured by two-dimensional Simpson's biplane method. About diastolic function, averaged E/E' (early peak mitral inflow velocity/peak mitral annular velocity ratio) was calculated as non-invasive estimation of LV filling pressure.

### Statistical analysis

All analyses were performed using SPSS statistic software (version 25) for Windows. Continuous variables were expressed as mean with standard deviation (SD), while categorical variables were presented as number of cases and percentage. The entire patient population was stratified by sex (males and females). Moreover, basing on the median age of 68 years (interquartile range 60 - 75 years), the total population was also stratified in adult (< 68 years old) and old ( $\geq$  68 years old) patients, so that four groups were finally obtained: males < 68 yrs old, males  $\geq$  68 yrs old, females < 68 yrs old, females  $\geq$  68 yrs old. All types of cardiac surgeries were grouped into four general categories: isolated coronary artery bypass graft (CABG), combined CABG and any valve surgery (CABG+Val), valve surgery (Valve surg), other, including surgery for aortic aneurysm or dissection, ventricular shaping, LV assistance device, grow-up congenital heart disease.

Valve surgery category included both repair and replacement, with either mechanical or biologic prosthesis, and was intended for single or multiple valves. Complications were differentiated into complications occurring immediately after surgery, but before admission in CR (Post-OP complications), and complications occurring during CR (Complications during CR).

Moreover, based on values of LV EF at admission, patients were stratified in those with preserved EF (i.e. EF  $\geq$  50%) and impaired EF (i.e. EF  $<$  50%), as recommended by current guidelines [17]. Intragroup comparisons between admission and discharge were performed by one-way ANOVA for repeated measures. Interaction of trends in performance indexes with age and sex was checked by two-way ANOVA for repeated measures. Comparisons between groups were determined by unpaired T-test for continuous variables and by Chi-squared test for categorical variables. Statistical significance was defined as  $p \leq 0.05$  (2 sided).

## Results

### Clinical and demographic characteristics

Out of 732 patients initially considered for enrolment, 55 patients were subsequently excluded by analysis because of missing data (7 patients) or because CR program had to be prematurely stopped due to serious complications requiring transfer in an intensive care unit or cardiology ward (48 patients). Thus, 677 patients admitted after cardiovascular surgery and discharged at home made the final study population. Clinical data are presented in table 1.

In the overall study population, mean age was  $66 \pm 12$  years and mean length of stay was  $13 \pm 5$  days. There was prevalence for male sex (73% vs 27% female,  $p < 0.001$ ), while adult and elderly patients were balanced (48.8% and 51.2%, respectively,  $p = ns$ ) in the overall study population and among men and women. Hypertension and diabetes were more prevalent in elderly than in adult women (85% vs 56%,  $p < 0.001$  and 40% vs 26%,  $p = 0.041$ , respectively), with no significant age-related differences among men. Adult men had more smoking habits than adult women (59% vs 37%,  $p = 0.008$ ). Incidence of Post-OP and during CR complications was similar in men and women (25.7% vs 27.2%;  $p = ns$  and 10.8% vs 14.4%;  $p = ns$  respectively) and generally was prevalent in elderly compared to adult male patients (Table 1), without any difference of age among women.

Significant gender-related differences emerged in type of surgery done: valve surgery was more prevalent in females than in males, irrespectively of age (54% vs 30%, respectively, in patients  $< 68$  yrs,  $p < 0.001$ ; 69% vs 33%, respectively, in patients  $\geq 68$  yrs,  $p < 0.001$ ). Conversely, CABG was less frequent in females than in males, irrespectively of age (23% vs 52%, respectively, in patients  $< 68$  yrs,  $p < 0.001$ ; 30% vs 52%, respectively in patients  $\geq 68$  yrs,  $p < 0.001$  (Table 1). In both sexes, other cardiac surgeries were more frequent in adult than in elderly patients (9% vs 4%, respectively, in males,  $p = 0.016$ ; 18% vs 4%, respectively, in females,  $p = 0.002$ ). However, adult women underwent more frequently other surgeries than their male counterpart (18% vs 9%, respectively,  $p = 0.042$ ). Post-OP complications occurred more frequently in elderly men than in adult men (31% vs 20%,  $p = 0.005$ ), while no difference was found among women. Complications during CR occurred with the same frequency in both sex and age groups (Table 1).

Length of hospital stay was longer in elderly than in adult patients both among males and females ( $p = 0.017$  and  $p = 0.018$ , respectively). Notably, elderly females had longer hospital stays than old males ( $p = 0.008$ ). Number of exercise sessions was  $9.4 \pm 3.3$  days in male and  $9.9 \pm 3.6$  days in female patients ( $p = 0.074$ ), and it was slightly longer in elderly patients ( $10 \pm 4.1$  vs  $9.4 \pm 3$  in patients  $< 68$  years;  $p = 0.025$ ).

### Trends of physical performance indexes according to sex and age

Interaction with sex and age was significant for metres walked during 6-minute walking test ( $p = 0.004$  for sex interaction,  $p < 0.001$  for age interaction). Particularly, improvement of such performance index by CR was lower for women than men, although metres walked

	Total Population (n = 677)					
	Male (n = 497, 63%)			Female (n = 180, 27%)		
	< 68 yrs (n = 252, 51%)	≥ 68 yrs (n = 245, 49%)	P	< 68 yrs (n = 78, 43%)	≥ 68 yrs (n = 102, 57%)	P
Hypertension, n (%)	183 (73)	185 (75)	ns	44 (56)‡	87 (85)‡‡	< 0.001
Diabetes, n (%)	60 (24)	77 (31)	0.057	20 (26)	41 (40)	0.041
Dyslipidemia, n (%)	134 (53)	125 (51)	ns	33 (42)	59 (58)	0.039
Smoking, n (%)	148 (59)	123 (50)	0.056	29 (37)**	41 (40)	ns
Obesity, n (%)	53 (21)	38 (16)	ns	16 (20.5)	20 (20)	ns
Length of stay, days, mean ± SD	13 ± 4	14 ± 5	0.017	13.7 ± 5.1	15.6 ± 5.5**	0.018
HF symptoms at admission, n (%)	10 (4)	21 (8.5)	0.034	5 (6)	4 (4)	ns
HF symptoms at discharge, n (%)	0	0		0	0	
CABG, n (%)	131 (52)	127 (52)	ns	18 (23)*	31 (30)*	ns
CABG+Valv, n (%)	18 (7)	23 (9)	ns	2 (2.5)	4 (4)	ns
Valve Surg, n (%)	76 (30)	82 (33)	ns	42 (54)*	60 (59)*	ns
Other surg, n (%)	24 (9)	10 (4)	0.016	14 (18)†	4 (4)	0.002
Postoperative complications, n (%)	51 (20)	77 (31)	0.005	21 (27)	28 (27)	ns
Complications during rehabilitation, n (%)	24 (9)	30 (12)	ns	9 (11.5)	17 (17)	ns
Statistical significance vs male: *p < 0.001; **p = 0.008; †p = 0.042; ‡p = 0.007; ‡‡p = 0.044; §p = 0.002 vs male						

Table 1

increased for both sexes from admission to discharge (p < 0.001): indeed, female patients were able to walk a lower distance compared to male both at admission and at discharge (p < 0.001 for both) (Figure 1, panel A). Similarly, metres walked increased in both adult and elderly patients from admission to discharge (p < 0.001 for both), but performance was less efficient for elderly than for adult patients at each time point (p < 0.001) (Figure 2, panel A).

Perception of effort did not show sex and age-related differences (p = ns for interaction). It significantly improved in both sexes from admission to discharge (p < 0.001 for both), but was harder in female than male patients (p = 0.001) at admission (Figure 1, panel B) and elderly than adult patients both at admission (p < 0.001) and at discharge (p = 0.008) (Figure 2, panel B).

Barthel scale of ability in daily life activities was more compromised in females than males at both admission (p < 0.001) and discharge (p = 0.006), but it equally improved in both sexes by CR (p < 0.001 for both), with no significant sex-related differences (Figure 1, panel C). Similarly, Barthel index improved after CR in both adult and elderly patients (p < 0.001), with no age-related differences. However, elderly were more compromised than adult at admission (p < 0.001) and remained more compromised also at discharge (p = 0.006) (Figure 2, panel C).

At admission, VO<sub>2</sub> max was lower in female (Figure 1, panel D) and elderly (Figure 2, panel D) patients than in their counterparts (p < 0.001 for both comparisons). It improved at the end of in-hospital CR, without significant gender and age-related differences.

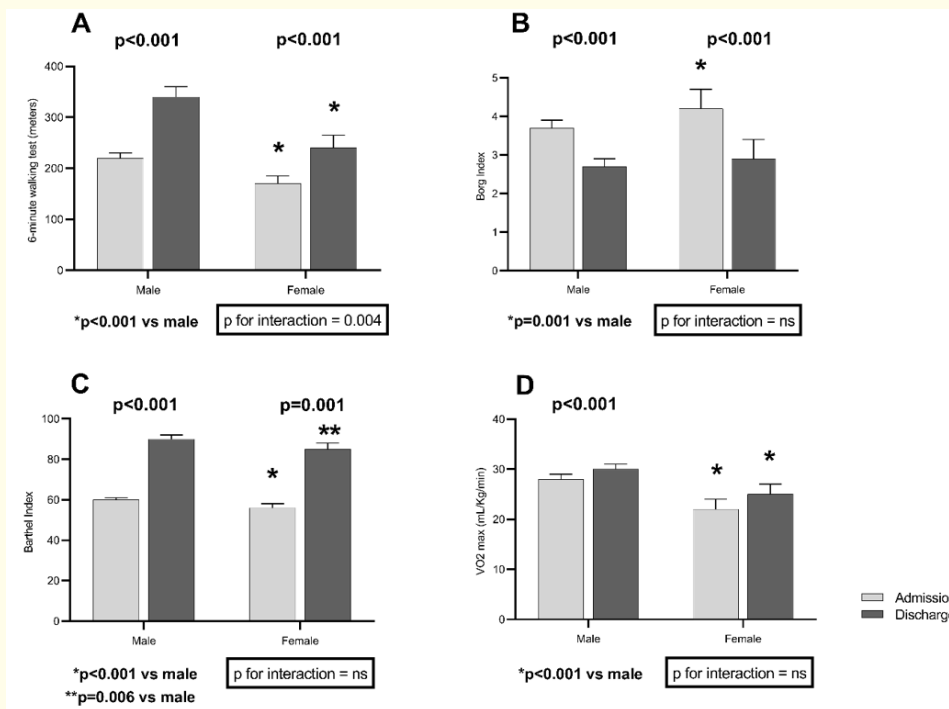


Figure 1: Values of physical performance at admission in CR (light grey) and discharge (dark grey), stratified by sex: 6-minute walking test (a), Borg index (b), Barthel index (c) and VO<sub>2</sub> max (d).

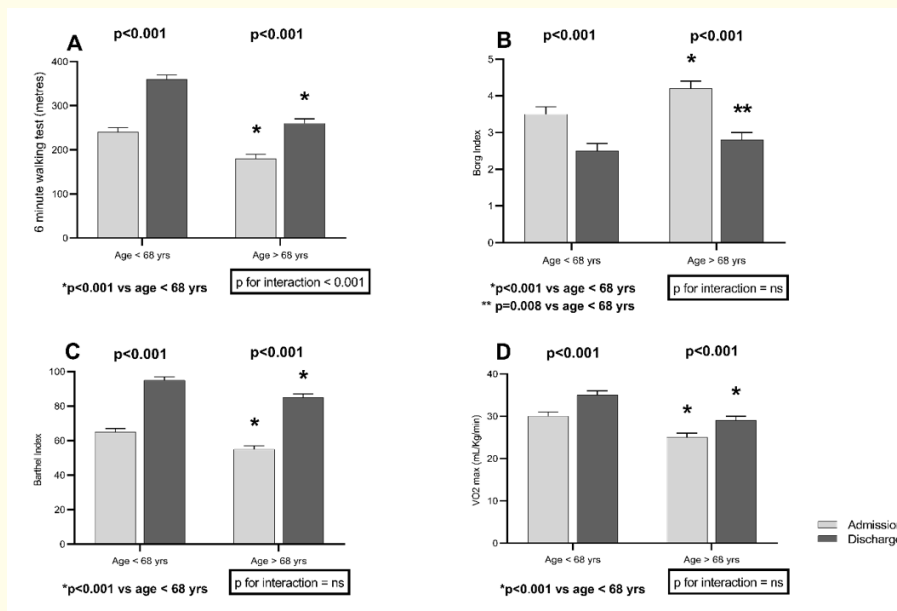


Figure 2: Values of physical performance at admission in CR (light grey) and discharge (dark grey), stratified by age: 6-minute walking test (a), Borg index (b), Barthel index (c) and VO<sub>2</sub> max (d).

After stratification for type of surgery, no significant gender-related differences were found in trend of performance indexes among patients treated by CABG+Valve Surgery and Other Surgery (Table 2). However, among patients undergoing CABG, women were more compromised than men at admission for all performance parameters. After CR, women improved similarly than men, except for Borg index, which, independently of length of stay, type of exercise performed and cardiovascular risk factors, improved more in women than in men (p = 0.002 for interaction). Also, among patients undergoing valve surgery, women were more compromised than men in all performance indexes at admission and improved after CR, but significantly less than men in 6-minute walking test (p = 0.004 for interaction). Elderly performed worse than adult patients at admission in every type of surgery group. After CR, they improved by the same extent of their adult counterparts in all but in Barthel index after valve surgery (p = 0.049 for interaction), and in 6-minutes walking test after other surgeries (p = 0.058 for interaction), whereas they took more advantage than adult in Borg index after other surgery and (p = 0.032 for interaction) (Table 3).

	Total population (n = 678)				p for interaction (ANOVA ¥)
	Male (n = 497)		Female(n = 180)		
CABG	Admission	Discharge	Admission	Discharge	
6-minute WT, metres, mean ± SD	223.88 ± 83.57	331.47 ± 134.91	147.26 ± 72.18*	227.08 ± 118.99*	ns
BORG index, mean ± SD	3.42 ± 2.02	2.53 ± 1.76	4.63 ± 2.52*	2.82 ± 1.99	0.002
BARTHEL index, mean ± SD	59.98 ± 15.78	90.89 ± 22.92	53.43 ± 15.20**	84.39 ± 23.01	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.99 ± 1.01	3.35 ± 1.02	2.32 ± 9.51*	2.70 ± 8.36*	ns
<b>CABG + Valve Surgery</b>					
6-minute WT, metres, mean ± SD	201.17 ± 79.79	307.39 ± 138.18	137.33 ± 48.82	236.16 ± 120.22	ns
BORG index, mean ± SD	4.97 ± 2.18	2.78 ± 1.75	4.33 ± 2.06	2.5 ± 1.87	ns
BARTHEL index, mean ± SD	58.27 ± 12.78	86.93 ± 26.99	53.83 ± 5.91	89.67 ± 9.69	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.70 ± 9.82	3.12 ± 9.62	2.20 ± 8.76	2.83 ± 7.42	ns
<b>Valve Surgery</b>					
6-minute WT, metres, mean ± SD	221.27 ± 82.02	343.48 ± 134.18	169.86 ± 71.70*	243.09 ± 136.05*	0.004
BORG index, mean ± SD	3.74 ± 2.30	2.87 ± 1.76	4.39 ± 2.29***	3.12 ± 2.35	ns
BARTHEL index, mean ± SD	61.77 ± 13.55	93.83 ± 17.20	56.37 ± 14.79§	85.81 ± 24.60§§	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.80 ± 8.57	3.18 ± 9.03	2.21 ± 6.84*	2.54 ± 7.72*	ns
<b>Other Surgery</b>					
6-minute WT, metres, mean ± SD	237 ± 94.82	358.0 ± 163.0	202.33 ± 70.40	293.33 ± 184.55	ns
BORG index, mean ± SD	4.18 ± 2.23	2.94 ± 1.98	3.78 ± 2.46	2.17 ± 1.89	ns
BARTHEL index, mean ± SD	64.18 ± 15.02	90.79 ± 24.66	60.11 ± 10.99	84.89 ± 31.44	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	3.14 ± 9.37	3.47 ± 9.36	2.64 ± 9.61	3.20 ± 9.73	ns
*p < 0.001 vs male			¥ adjusted for covariates: age, length of stay, type of exercise (Cyclette, Treadmill, Cyclette+Treadmill, Cyclette+Ergometer; Pedals), symptoms of heart failure at admission, left ventricular ejection fraction < 50%, hypertension, diabetes, dyslipidemia, obesity, smoking		
**p = 0.008 vs male					
***p = 0.026 vs male					
§p = 0.003 vs male					
§§p = 0.002 vs male					

Table 2

	Total population (n = 678)		Age ≥ 68 yrs (n = 347)		p for interaction (ANO-VA ¥)
	Age < 68 yrs (n = 330)		Age ≥ 68 yrs (n = 347)		
<b>CABG</b>	Admission	Discharge	Admission	Discharge	
6-minute WT, metres, mean ± SD	214.15 ± 8.3	314.89 ± 12.8	209.21 ± 7.9*	316.83 ± 12.23*	ns
BORG index, mean ± SD	3.7 ± 0.2	2.34 ± 0.2	3.5 ± 0.2	2.8 ± 0.2*	ns
BARTHEL index, mean ± SD	59.3 ± 1.6	89.1 ± 2.4	58.6 ± 1.5*	91.2 ± 2.2**	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.9 ± 1.2	3.2 ± 1.2	2.9 ± 1.2§	3.3 ± 1.2§	ns
<b>CABG + Valve Surgery</b>					
6-minute WT, metres, mean ± SD	141.1 ± 30.3	281.2 ± 51.7	231.5 ± 23.5*	311 ± 40*	ns
BORG index, mean ± SD	4.7 ± 0.8	3.4 ± 0.7	5 ± 0.6	2.25 ± 0.6*	ns
BARTHEL index, mean ± SD	51.7 ± 5.3	88.4 ± 10.2	62.1 ± 4.1*	86.5 ± 7.9**	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.8 ± 0.43	2.78 ± 0.42	3.1 ± 0.35§	3.35 ± 0.34§	ns
<b>Valve Surgery</b>					
6-minute WT, metres, mean ± SD	194.9 ± 8.7	319.4 ± 15.2	206.2 ± 7.5*	291.4 ± 13.2*	ns
BORG index, mean ± SD	4 ± 0.3	3.1 ± 0.3	4.1 ± 0.25*	2.9 ± 0.23	ns
BARTHEL index, mean ± SD	58.2 ± 1.6	93.7 ± 2.5	60.8 ± 0.44*	88.15 ± 2.1*	0.049
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	2.6 ± 0.11	3.0 ± 0.11	2.6 ± 0.10*	2.92 ± 0.10*	ns
<b>Other Surgery</b>					
6-minute WT, metres, mean ± SD	230.2 ± 13.4	374.3 ± 29.5	210.8 ± 28.3†	230.5 ± 58.8††	0.058
BORG index, mean ± SD	3.6 ± 0.4	3.1 ± 0.3	5.3 ± 0.8	1.6 ± 0.7	0.032
BARTHEL index, mean ± SD	63 ± 2.35	91.12 ± 4.66	62.09 ± 4.78	82.11 ± 9.47	ns
VO <sub>2</sub> max, mL/Kg/min, mean ± SD	3.06 ± 0.2	3.45 ± 0.2	2.9 ± 0.43	3.34 ± 0.43	ns
*p < 0.001 vs Age < 68 yrs **p = 0.006 vs Age < 68 yrs §p = 0.002 vs Age < 68 yrs †p = 0.032 vs Age < 68 yrs ††p = 0.025 vs Age < 68 yrs			¥ adjusted for covariates: sex, length of stay, type of exercise (Cyclette, Treadmill, Cyclette+Treadmill, Cyclette+Ergometer, Pedals), symptoms of heart failure at admission, left ventricular ejection fraction < 50%, hypertension, diabetes, dyslipidemia, obesity, smoking		

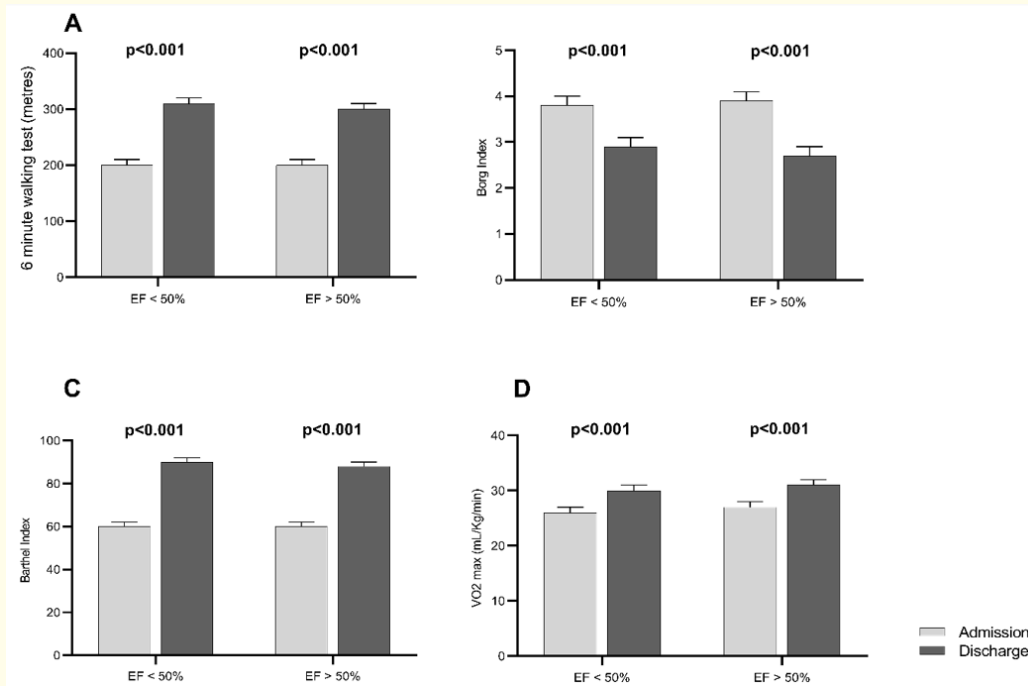
Table 3

**Trends of physical performance indexes according to LV EF**

No differences were observed in terms of age, number of exercise sessions and length of stay in patient with EF < 50% (n = 162, 24%) and ≥50% (n = 516, 76%). Performance indexes improved by CR, regardless of EF (Figure 3). No interactions between sex/age and EF were found.

**Improvement of echocardiographic data by exercise**

Although both patients with preserved and reduced LV contractile function took advantage from CR by improving EF (p < 0.001), CR was more beneficial in patients with depressed EF at admission (p < 0.001 for interaction): indeed, relative increment in myocardial



**Figure 3:** Values of physical performance at admission in CR (light grey) and discharge (dark grey), stratified by left ventricular ejection fraction (EF): 6-minute walking test (a), Borg index (b), Barthel index (c) and VO2 max (d).

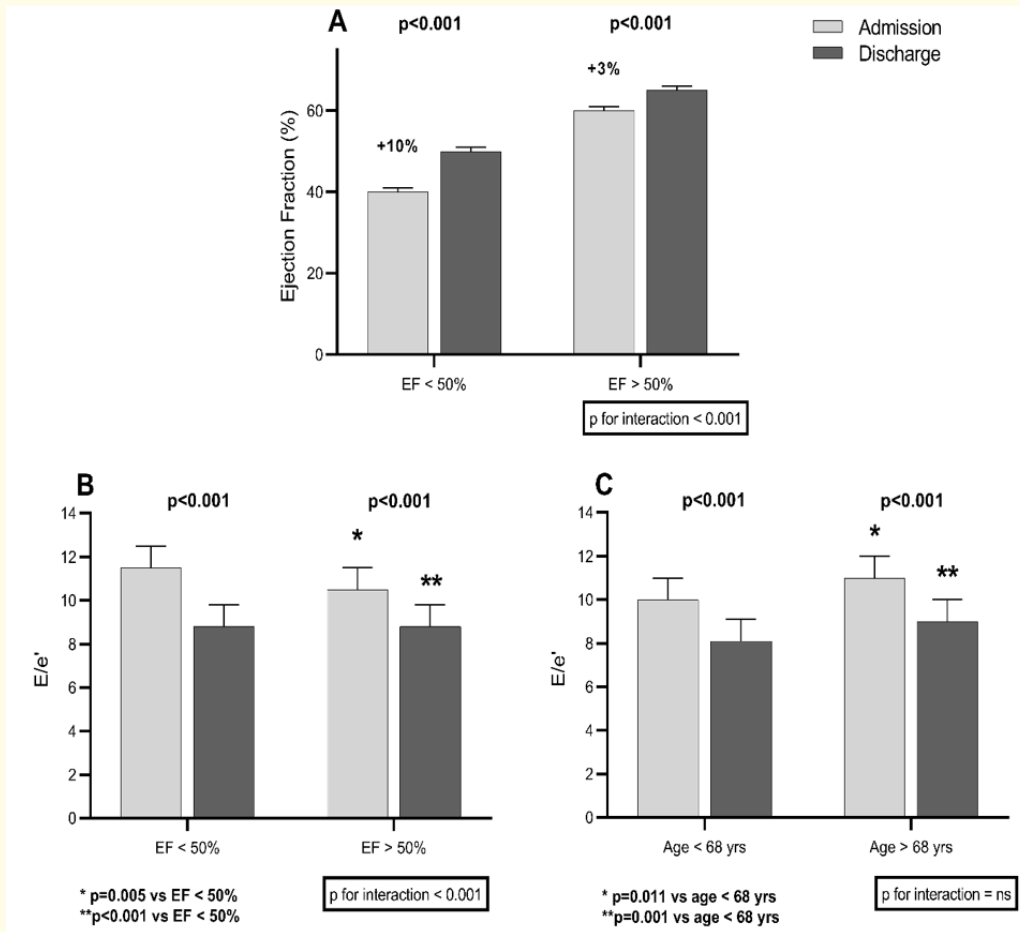
performance was greater in those with LV EF < 50% (10% vs 3% in patients with LV EF ≥ 50%, p = 0.0002) (Figure 4, panel A). LV filling pressure also improved after CR in both EF groups (p < 0.001), and even more in patients with LV EF < 50% (p < 0.001 for interaction) (Figure 4, panel B), as patients with preserved EF had better values of E/E' both at admission (p = 0.005) and at discharge (p < 0.001).

Trend in LV filling pressure did not show age-related neither sex-related differences, as elderly patients presented higher LV filling pressure at admission compared to adult patients (p = 0.011) but recovered similarly during CR (p = ns for interaction) (Figure 4, panel C).

## Discussion

This study describes the functional characteristics and in-hospital outcome of a large post cardiac surgery patient population of a CR unit. At admission in CR, women behave similarly to elderly patients, as both groups are functionally more compromised than their counterpart, respectively. Although CR program produces significant improvement in symptoms and functional capacity in all patients' categories, neither women, nor elderly patients reach the levels of men and adult patients, respectively. Relative increment in physical and subjective wellness was similar for both sexes, with sex-related differences only about 6-minute walking test. Similarly, age-related differences regarded only 6-minute walking test, in which CR produced less improvement in elderly than in adult patients. Notably, no age-related differences were found in the other physical and subjective wellness indexes, thus indicating that CR produces benefits by the same extent, regardless of age. Furthermore, patients with reduced EF at admission took more advantage from CR program than patients with preserved EF, as improvement of systolic and diastolic function was greater in the former than in the latter.





**Figure 4:** Comparison of LV EF values at admission in CR (light grey) and discharge (dark grey) in patients with preserved and reduced LV systolic function (a). Trends in E/e' values at admission in CR (light grey) and discharge (dark grey), according to LV EF groups (b) and age (c). EF = Ejection Fraction; LV = Left Ventricle.

**Post-surgery cardiac rehabilitation**

After heart surgery, CR is an essential therapeutic procedure, able to improve survival even up to 20%<sup>1</sup>. The first task of a CR team is to manage all the possible post-surgery complications, such as arrhythmias, anaemia, infections, heart failure. Once clinically stabilized, deconditioned patients need to recover their muscular strength and function, with correct nutrition and exercise. Respiratory exercise is performed everyday by all patients. Then, after functional evaluation performed using a 6-minute WT, patients may engage in an appropriately designed exercise protocol, in order to improve functional capacity. Throughout all hospital stay, all patients receive education on risk factors reduction and their preventive strategies, basic knowledge on the use of major cardiovascular drugs, healthy life-style changes, correct nutrition, management of surgical wounds, physiotherapeutic measures to maintain fitness. Last, but not least, all patients undergo psychological evaluation and short-term treatment in case of anxiety and depression, both as expression of post-acute event stress or as exacerbation of pre-existent disease. Such evaluation is also crucial in order to optimize patient’s adherence to rehabilitation

protocol. At discharge, functional and clinical improvement is assessed in all patients by 6-minute WT. A personalized exercise prescription is provided in all patients, which takes into account heart function, desirable heart rate response during exercise and osteo-artro-muscular fitness.

Thus, in-hospital CR is the result of a multidisciplinary and multiprofessional team, able to provide significant improvement in functional status, quality of life and survival of cardiac patients.

### Gender and age-related issues in cardiac rehabilitation

Significantly less represented within the CR patient population, female patients are functionally more compromised than men and, although their improvement in  $VO_2$  max, Barthel and Borg indexes is similar to their male counterpart, they never reach the same level of performance. Rather, their relative improvement in metres walked in 6 minutes is lower than that of male patients undergoing similar CR program, thus indicating that recovery of physical capacity after cardiac surgery is actually demanding for women. As result, women in CR behave as elderly patient, beginning with lower performance and increasing to a lower final level after CR cycle. The reasons for this difference remain to be elucidated, and they reside probably on the major weakness of osteo-artro-muscular apparatus along with more sedentary lifestyle.

Whether longer CR program would allow women to reach a better fitness level, similar to men, is currently unknown. Thus, all patients, particularly women and elderly, should be encouraged to engage in-house CR.

Surely, further considerations and studies are needed on the role of pre-habilitation in women and elderly. In fact, given the low fitness and performance level of female and elderly patients, it is conceivable, that, in the absence of specific contraindications, these patients' categories might benefit from CR program aimed to improvement of strengthening, nutrition, and respiratory function. Cardiac Rehabilitation (CR) after cardiac surgery is underutilized in female and elderly patients.

According to our results, CR projects should be personalized not only in terms of modalities, volume and intensity of exercise, but also according to the length of hospital stay, taking into consideration gender and age physical fitness peculiarities.

### Benefits of CR on LV myocardial performance

CR is known to improve also cardiac function after an acute cardiac event [18]. Effects of CR on LV myocardial performance after any cardiac surgery are controversial, mainly because insufficient data have been reported in the literature [19]. In a survey [20] on patients treated by mitral or aortic valve surgery, no survival advantage existed for patients with normal preoperative EF who attended CR, compared to patients not participating in CR program. In our study population, benefits of CR on physical performance were evident irrespectively of EF. By paralleling, amelioration of LV contractile function was found in our patients with both  $EF < 50\%$  and  $EF \geq 50\%$ : as noteworthy, the relative increment was greater in patients with reduced EF and was surprisingly high. Our findings are in keeping with results of a study conducted in Pakistani patients with LV  $EF < 50\%$  or  $> 50\%$  treated by CABG, in whom exercise training program enhanced exercise capacity linked with recovery of cardiac function [21].

Fewer previous data exist about variation of LV diastolic function, particularly  $E/E'$ , induced by CR. In patients with myocardial infarction treated by percutaneous revascularization,  $E/E'$  remains unchanged after CR [22]. In our study,  $E/E'$  at admission in CR was greater in patients with reduced LV EF and with age  $\geq 68$  years and significantly decreased after CR. Elevated LV filling pressure are often associated

to LV contractile dysfunction due to ischemic cardiomyopathy and valvular heart disease, both of them potentially reversing up to several months after surgery. On the contrary, greater E/E' values in old than young patients have been described as physiological phenomenon in normal subjects of both sexes, mainly due to progressive aging and stiffening of LV myocardium [23]. The absolute novelty of our study resides into demonstration that, also in old patients, E/E' may be decreased by CR, similarly to what happens in young patients. This indicates that LV stiffening is not fixed and irreversible. Pathophysiological bases of such phenomenon are currently unknown, but therapeutic implications of CR may be relevant.

### Conclusion

During CR after any cardiac surgery, women behave similarly to elderly patients, as both groups are functionally more compromised than their counterpart at baseline and do not reach the levels of men and younger patients, respectively, despite significant improvement in symptoms and functional capacity. Thus, significant age-related differences in physical capacity and subjective wellness exist, as elderly patients generally recover less than young patients. Since women and elderly are less referred to CR programs in clinical practice, the results of this study should encourage physician to propose in-house CR to these functionally compromised patients. Whether longer CR program would allow women to reach a better fitness level, similar to men, is currently unknown. Thus, CR projects should be personalized not only in terms of modalities, volume and intensity of exercise, but also according to the length of hospital stay, taking into consideration gender and age physical fitness peculiarities.

### Disclosure

All authors declare no conflicts of interest.

All authors have read and approved submission of the manuscript and the manuscript has not been published and is not being considered for publication elsewhere in whole or part in any language except as an abstract.

### Acknowledgements

We acknowledge the hard work of sonographer Federica Palma for technical support in data analysis and management.

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**Volume 8 Issue 11 November 2020**

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