




# Determinants of Functional Improvement After Cardiac Rehabilitation in Acute Coronary Syndrome

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## Abstract

**Introduction** Cardiac rehabilitation (CR) is an effective tool for secondary prevention after acute coronary syndrome (ACS).

**Aim** Aim of our study was to find the significant determinants of exercise capacity (evaluated with the six-minute walking test—6-MWT) and functional improvement in patients undergoing CR after an ACS.

**Methods** The study group included 298 patients (mean age  $61.6 \pm 10.2$  years; males 80.2%) who, after ACS, were enrolled in CR program at Niguarda Hospital in Milan from 2015 to 2018. For all patients, we collected anamnestic, clinical and instrumental cardiological data. All patients performed a 6-MWT at the beginning (6-MWT-1) and at the end (6-MWT-2) of CR program.  $\Delta$  meters were used to represent functional improvement.

**Results** Multiple linear regression models were carried out for 6-MWT-1, 6-MWT-2,  $\Delta$  meters and %  $\Delta$  meters. Standardized regression coefficients showed that age ( $\beta = -0.237$ ;  $p < 0.001$ ), BMI ( $\beta = -0.116$ ;  $p = 0.006$ ) and heart rate ( $\beta = -0.082$ ;  $p = 0.040$ ) were determinants of exercise capacity (6MWT-1 and 2), whereas age ( $\beta = -.231$ ;  $p = 0.004$ ), sex ( $\beta = -0.187$ ;  $p = 0.008$ ) and BMI ( $\beta = -0.164$ ;  $p = 0.022$ ) were determinants of functional improvement ( $\Delta$  meters).

**Conclusions** Our data showed that functional improvement after CR in ACS patients is mainly related to non-cardiological variables. Instead it is related to intrinsic factors, both modifiable (BMI) and non-modifiable (age, sex).

**Keywords** Cardiac rehabilitation · Acute coronary syndrome · Functional improvement

## 1 Introduction

Advances in the treatment of Acute Coronary Syndrome (ACS) achieved in the last decades led to an improvement in patient survival and, consequently, generated the need to intervene in terms of secondary prevention and Cardiac Rehabilitation (CR). Furthermore, since the duration of hospitalization is being reduced and the attention is more focused on the resolution of the acute problem, CR responds

to the need to implement other types of intervention, such as health education and information, promotion of lifestyle changes, monitored physical activity, therapeutic optimization, risk stratification, functional and global evaluation [1]. CR health education interventions are particularly of interest to improve awareness of CV risk factors [2] and adherence to medical therapies [3]. CR participation after an ACS has demonstrated to be effective in reducing subsequent mortality [4].

Different and discordant associations between baseline characteristics of patients undergoing CR after ACS and their functional improvement could be found in literature. Lower exercise capacity at baseline, advanced age, higher lipids, female sex, and higher BMI have been found to be negative predictors of functional improvement after CR [5–11]. However also data showing that the improvement was not related to age, sex or left ventricular function [12, 13] have been published. Thus, the aim of our study was to define the determinants of functional improvement in

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patients undergoing CR after ACS. In order to quantify exercise capacity and functional improvement, patients performed a Six-Minute Walking Test (6-MWT) at the beginning and at the end of CR.

## 2 Methods

### 2.1 Study Population

A total of 410 consecutive patients were enrolled in the CR program of the Niguarda Hospital (Milan, Italy) institution from January 1st 2015 to December 31st 2018. Exclusion criteria were all non-ACS heart diseases (Chronic Coronary Syndrome, dilated or hypertrophic cardiomyopathy and peripheral artery disease) as well as neurological, pneumological or orthopaedic diseases impairing prolonged physical activity. Furthermore, individuals with a premature interruption of CR program were not considered in our study.

After application of exclusion criteria, 298 patients (239 men and 59 women) who were included in the CR program starting within two weeks after the index ACS were analysed (Fig. 1).

We collected data on medical history and physical examination at the beginning of the CR program, including age, body mass index (BMI), risk factors (hypertension, Diabetes Mellitus—DM—smoking habit and dyslipidaemia), pharmacotherapy (focusing on  $\beta$ -blockers, lipid-lowering,

antiplatelet and antihypertensive drugs) and details on CV diseases, such as previous percutaneous or surgical revascularisation, number of critically occluded coronary vessels and maximum high-sensitivity cardiac troponin (hs-cTnT) and creatine kinase MB isoenzyme (CK-MB) values achieved during the event.

Moreover, we investigated the pharmacological history, in particular for the following classes of drugs:  $\beta$ -blockers, lipid-lowering, antiplatelet and antihypertensive drugs.

We also registered findings about blood pressure (BP), heart rate (HR) and left ventricular ejection fraction (LVEF) documented at the echocardiogram both at the beginning and at the end of the CR program, as we did with blood tests such as total-cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, glucose and creatinine.

### 2.2 Cardiac Rehabilitation Program

The training program included 25 sessions with a total amount of 5 weeks of CR, which was performed in an outpatient setting in order to provide high intensity rehabilitation services and low intensity clinical care.

The daily aerobic physical exercise, which was the main activity of the program, was divided into 45 min of endurance training on the exercise bike and, after 15 min of resting time, 45 min of free-body exercises. Physical exercise intensity was modulated individually on functional capacity and effort tolerance.

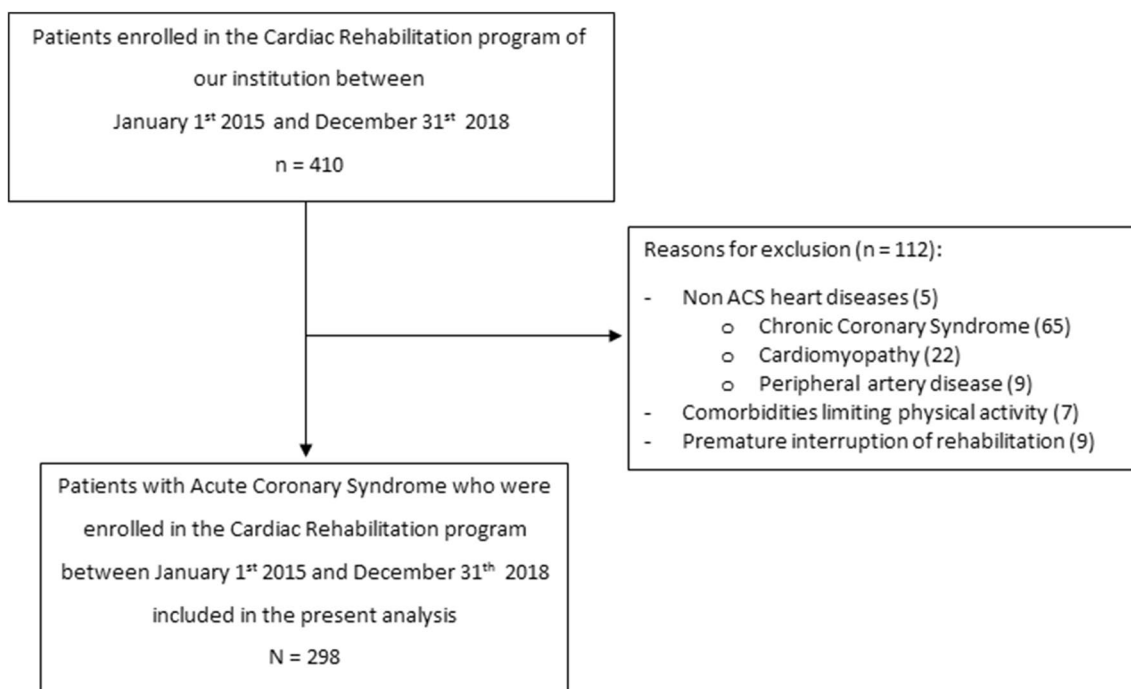


Fig. 1 Study flow-chart of patients included in the analysis. ACS acute coronary syndrome

Beside the cardiologist, who was the reference and coordinating figure, candidates related with a multidisciplinary team composed of nurses and physiotherapists. Moreover, CR program included a clinical dialogue with a psychologist—aiming to support the patient in changing lifestyle and in controlling emotional feelings—and dietology consultation in order to educate about nutritional habits.

### 2.3 Six-Minute Walking Test

Each candidate was submitted to a 6-MWT under standardized conditions, consisting in a 30 m, straight indoor hallway in accordance with the ATS guidelines [14]. Data registered on 6-MWT included vital signs (heart rate and oxygen saturation, detected at rest and at the end) and distance in meters.

The test was reproduced both at the beginning and at the end of the program, in order to obtain the functional improvement of the patient represented by the  $\Delta$  meters, resulting from the mathematical subtraction of the distance covered at the end of CR and the one reached at the beginning. This indicator was also normalized for expected values, calculated using the following formula:

$$\text{Males : } (7.57 \times \text{height in cm}) - (5.02 \times \text{age}) - (1.76 \times \text{weight in kg}) - 309$$

$$\text{Females : } (2.11 \times \text{height in cm}) - (5.78 \times \text{age}) - (2.29 \times \text{weight in kg}) + 667$$

The tests were performed for all the patients at the two time point by a single trained physiotherapist.

The American Thoracic Society Guidelines suggest using absolute values when expressing the difference in distance travelled [15]; this recommendation is due to the lack of a definite indication about the use of the crude differences of the distance (m), its percentage or the values normalized for the expected one.

### 2.4 Statistical Analysis

Continuous and categorical variables were presented respectively as mean  $\pm$  Standard Deviation (SD) and percentages. A Paired Samples *T*-Test was used to compare baseline and final factors for continuous variables, while a Chi-Square Tests was performed for categorical ones. Similarly, comparisons between subgroup (according to  $\Delta$  meters and sex) were conducted using Independent Samples *T*-Test for continuous variables and Chi-Square Tests for categorical variables.

Pearson product-moment correlation coefficient or Spearman's rank correlation coefficient was used to assess correlations among variables as appropriate. Multivariable

linear regression models were performed considering the distance walked at 6-MWT at the beginning and at the end of CR and the relative  $\Delta$  meters (which was also normalized for expected values) as the dependent variables, respectively; independent predictors were selected including the most clinically important baseline variables characterized by statistically significance Pearson correlation coefficients (see methods section).

Statistical analyses were performed using SPSS Statistics (IBM®). A *p*-value < 0.05 was considered to determine statistical significance.

## 3 Results

### 3.1 Population Characteristics

Table 1 shows population characteristics. 80.2% of the study population were male and mean age was  $61.6 \pm 10.2$  years. Regarding CV risk factors BMI was  $26.9 \pm 3.7$  kg/m<sup>2</sup> so 57.7% of population were in overweight or obesity conditions, 16.1% were diabetic, 67.8% present dyslipidemia and 65.1% had arterial hypertension (with mean Systolic and Diastolic BP—SBP/DBP respectively— $122.1 \pm 15.4$  and  $74.8 \pm 10.2$  mmHg).

18.8% had received a previous coronary revascularisation (prior to the recent ACS) while, regarding the acute CV events that lead to CR, maximum CK-MB and TnT-hs

**Table 1** Population characteristics

Number	298
Male (%)	80.2%
Age (years)	$61.6 \pm 10.2$
BMI (kg/m <sup>2</sup> )	$26.9 \pm 3.7$
Overweight or obesity	57.7%
Diabetes mellitus	16.1%
Dyslipidaemia	67.8%
Arterial hypertension	65.1%
Smoking	63.4%
Previous coronary revascularization	18.8%
Atrial fibrillation	7.0%
CK-MB max (ng/ml)	$91.2 \pm 131.3$
TnT-hs max (ng/l)	$2344.4 \pm 4057.2$
Number of coronary arteries treated with stenting during index ACS	
1. Coronary artery	52.7%
2. Coronary arteries	27.9%
3. Coronary arteries	14.4%

*BMI* Body Mass Index, *CK-MB* creatine kinase MB fraction, *TnT-hs* troponin T high sensitive, *LDL* low density lipoprotein, *HDL* high density lipoprotein, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate

**Table 2** Clinical data at the beginning and at the end of CR program

	Baseline	Final	<i>p</i> value
Creatinine (mg/dl)	1.04 ± 0.42	1.07 ± 0.49	0.093
Total cholesterol (mg/dl)	177.3 ± 42.3	136.1 ± 28.9	< 0.001
LDL cholesterol (mg/dl)	110.3 ± 39.3	68.3 ± 22.7	< 0.001
HDL cholesterol (mg/dl)	43.6 ± 11.3	45.1 ± 12.3	0.006
Triglycerides (mg/dl)	129.2 ± 70.4	118.8 ± 64.9	0.018
Glycaemia (mg/dl)	109.4 ± 27.0	108.1 ± 19.7	0.708
SBP (mmHg)	122.1 ± 15.4	113.8 ± 11.0	< 0.001
DBP (mmHg)	74.8 ± 10.2	66.1 ± 7.9	< 0.001
HR (bpm)	62.6 ± 7.6	60.6 ± 7.3	< 0.001
LVEF (%)	54.5 ± 7.2	56.7 ± 6.0	< 0.001
6-MWD (m)	474.7 ± 97.2	590.6 ± 108.0	< 0.001

*LDL* low density lipoprotein, *HDL* high density lipoprotein, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *LVEF* left ventricular ejection fraction, *6-MWD* 6-minute walk distance

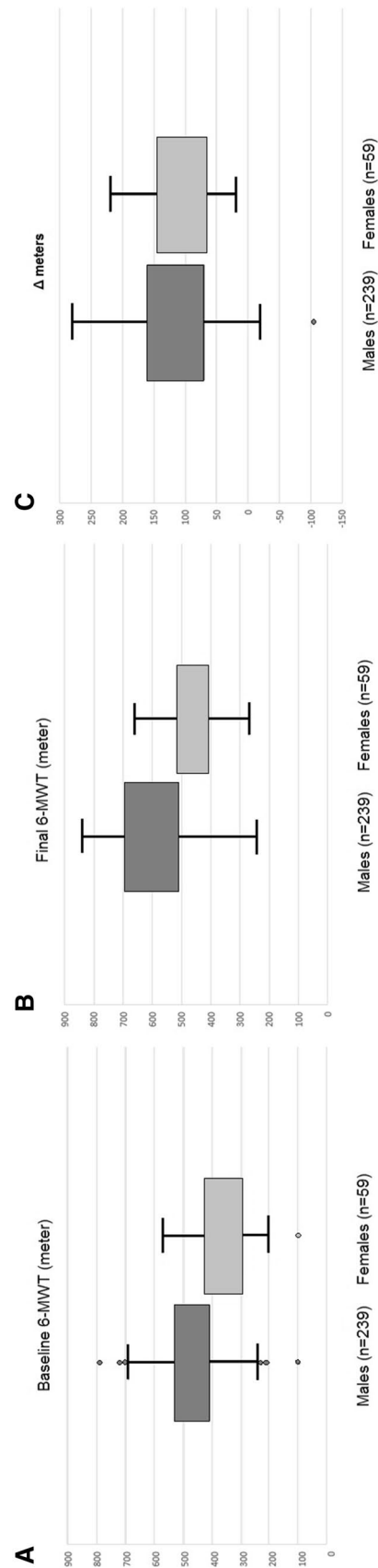
were  $91.2 \pm 131.3$  mcg/l and  $2344.4 \pm 4057.2$  ng/ml. 14.4% of subjects showed three critical coronary stenosis at the coronary angiography.

Baseline biochemical, echocardiographic and functional variables and their changes during CR were showed in Table 2. In the period between entry and discharge from CR, all patients improved the distance covered during the 6-MWT ( $474.7 \pm 97.2$  vs  $590.6 \pm 108.0$  m;  $p < 0.001$ ), configuring an average  $\Delta$  meters of  $115.8 \pm 59.2$ . Patients also improved lipid profile: total-cholesterol from  $177.3 \pm 42.3$  to  $136.1 \pm 28.9$  mg/dl ( $p < 0.001$ ); LDL-cholesterol from  $110.3 \pm 39.3$  to  $68.3 \pm 22.7$  mg/dl ( $p < 0.001$ ); HDL-cholesterol from  $43.6 \pm 11.3$  to  $45.1 \pm 12.3$  mg/dl ( $p = 0.006$ ); triglycerides from  $129.2 \pm 70.4$  to  $118.8 \pm 64.9$  mg/dl ( $p = 0.018$ ). Furthermore, patients reduced BP (SBP from  $122.1 \pm 15.4$  to  $113.8 \pm 11.0$  mmHg,  $p < 0.001$ ; DBP from  $74.8 \pm 10.2$  to  $66.1 \pm 7.9$  mmHg;  $p < 0.001$ ) and HR (from  $62.6 \pm 7.6$  to  $60.6 \pm 7.3$  bpm;  $p < 0.001$ ) and increased LVEF (from  $54.5 \pm 7.2$  to  $56.7 \pm 6.0$  %;  $p < 0.001$ ).

### 3.2 Subgroup Analysis

When patients were divided according to their  $\Delta$  meters median value (110 m), subjects with lower functional improvement were older ( $63.4 \pm 10.7$  vs  $59.8 \pm 9.3$  years;  $p = 0.004$ ) and presented higher HR ( $64.2 \pm 7.9$  vs  $61.1 \pm 7.0$  bpm;  $p = 0.003$ ) as shown in Supplementary Table 1.

Supplementary Table 2 showed clinical data when patients were divided according to sex. Females presented significantly lower final 6-MWT ( $470.0 \pm 92.4$  vs  $586.6 \pm 110.8$  m;  $p = 0.038$ , Fig. 2B) and BMI ( $26.4 \pm 4.7$  vs  $27.3 \pm 3.7$  kg/m<sup>2</sup>;  $p = 0.015$ ) in comparison to males, while they present a higher baseline LDL cholesterol ( $113.2 \pm 47.3$  vs  $108.9 \pm 37.4$  mg/dl;  $p = 0.025$ ). Furthermore, also a



**Fig. 2** Boxplot continuous outcome variables referred as baseline 6-MWT (A), final 6-MWT (B) and  $\Delta$  meters (C). In boxplots the inner line indicates the median; the whiskers are located at the maximum and minimum observation (outside observations indicated with dots are those out of the  $1.5 \times$  interquartile range)

border-line lower  $\Delta$  meters ( $101.2 \pm 50.8$  vs  $119.6 \pm 60.7$ ;  $p = 0.061$ , Fig. 2C) was founded.

### 3.3 Correlations and Regression Analysis

Correlations for baseline and final 6-MWT distance and the relative  $\Delta$  were showed in Table 3. Summarizing them, all the three variables correlates with age, baseline LDL cholesterol and baseline HR. The initial and the final covered distance both correlates with most of classical CV risk factors (BMI, arterial hypertension and baseline SBP, current or previous smoking habit) and diseases (previous coronary revascularisation and atrial fibrillation). Baseline 6-MWT distance also correlates with TnT peak ( $r = 0.129$ ,  $p = 0.038$ ) while final 6-MWT distance showed significant correlation also with DM ( $r = -0.176$ ;  $p = 0.003$ ), reduction of LDL-cholesterol from the beginning to the end of CR ( $r = -0.262$ ;  $p < 0.001$ ) and baseline glycaemia ( $r = -0.147$ ,  $p = 0.025$ ). Finally,  $\Delta$  meters showed correlations also with sex ( $r = -0.125$ ;  $p = 0.035$ ), DM ( $r = -0.155$ ;  $p = 0.009$ ), glycaemia ( $r = -0.132$ ;  $p = 0.045$ ) and number of coronary arteries affected by critical stenosis ( $r = -0.134$ ;  $p = 0.024$ ).

Subsequently, linear regression analysis was performed (Table 4). In the model for baseline 6-MWT meter as dependent variables, age, sex, BMI, arterial hypertension, smoking, LDL-cholesterol, maximum peak of hs-cTnT, baseline SBP and HR and atrial fibrillation were used as covariates. With a total  $R^2$  of 0.335 the significant determinants were age ( $\beta = -0.452$ ;  $p < 0.001$ ), BMI ( $\beta = -0.199$ ;  $p = 0.002$ ) and HR ( $\beta = -0.151$ ;  $p = 0.013$ ).

**Table 4** Determinants of exercise capacity and functional improvement

	$\beta$	$p$ -value
Baseline 6-MWD		
Age	-0.452	< 0.001
BMI	-0.199	0.002
Baseline HR	-0.151	0.013
Final 6-MWD		
Baseline 6-MWD	0.707	< 0.001
Age	-0.237	< 0.001
BMI	-0.116	0.006
Baseline HR	-0.082	0.040
$\Delta$ meters		
Age	-0.231	0.004
Male	-0.187	0.008
BMI	-0.164	0.022

BMI Body Mass Index, HR heart rate, 6-MWD 6-minute walk distance

In the model for walked distance at final 6-MWT also DM and meters covered at baseline 6-MWT was inserted as covariates. With a total  $R^2$  of 0.791 the significant determinants were the baseline walked distance ( $\beta = 0.707$ ;  $p < 0.001$ ), age ( $\beta = -0.237$ ;  $p < 0.001$ ), BMI ( $\beta = -0.116$ ;  $p = 0.006$ ) and HR ( $\beta = -0.082$ ;  $p = 0.040$ ).

Finally, model for  $\Delta$  meters present age, sex, BMI, DM, baseline LDL-cholesterol, glucose level, SBP, HR and the number of coronary arteries affected by critical stenosis as covariates. With a total  $R^2$  of 0.185 the significant

**Table 3** Correlations between clinical data and baseline 6-MWD, final 6-MWD and  $\Delta$  meters.

	Baseline 6-MWD		Final 6-MWD		$\Delta$ meters	
	$r$	$p$ -value	$r$	$p$ -value	$r$	$p$ -value
Age	-0.488	< 0.001	-0.511	< 0.001	-0.194	0.001
Male	-	-	-	-	-0.125	0.035
BMI	-0.220	< 0.001	-0.237	< 0.001	-	-
Diabetes mellitus	-	-	-0.176	0.003	-0.155	0.009
Arterial hypertension	-0.226	< 0.001	-0.258	< 0.001	-	-
Smoking	0.163	0.005	0.147	0.013	-	-
Previous coronary revascularisation	-0.160	0.006	-0.126	0.033	-	-
TnT-hs	0.129	0.038	-	-	-	-
Coronary vessels critical occlusion	-	-	-	-	-0.134	0.024
LDL cholesterol	0.135	0.026	0.213	<0.001	0.160	0.009
$\Delta$ LDL cholesterol	-	-	-0.262	< 0.001	-	-
Baseline glycaemia	-	-	-0.147	0.025	-0.132	0.045
Baseline SBP	-0.157	0.013	-0.175	0.007	-	-
Baseline HR	-0.168	0.009	-0.273	< 0.001	-0.192	0.003
Atrial Fibrillation	-0.178	0.002	-0.187	0.001	-	-

BMI Body Mass Index, TnT-hs troponin T high sensitive, LDL low density lipoprotein, SBP systolic blood pressure, HR heart rate

determinants were age ( $\beta = -0.231$ ;  $p = 0.004$ ), sex ( $\beta = -0.187$ ;  $p = 0.008$ ) and BMI ( $\beta = -0.164$ ;  $p = 0.022$ ). Similar results were also founded when  $\Delta$  meters was normalized for the expected values.

## 4 Discussion

The main result of our study was that the determinants of functional capacity (both at the beginning and at the end of CR) were age, BMI and HR. Furthermore, sex is implicated as a determinant of functional improvement (i.e.  $\Delta$  meter) obtained during CR.

The relationship between older age and lower physical performance, both in terms of exercise capacity and functional improvement, is complex. First of all, age-related muscle change, which involves both skeletal muscle morphology and functionality, should be considered in older patients. Sarcopenia, the loss of muscle mass related to aging, physiologically occurs within the elderly population [5]. Furthermore, the interaction between older age and reduction of functional capacity can be confused with presence of comorbidities, which can negatively affect the execution of physical activity and the autonomy of the patient [5, 16]. Moreover, elderly patients are more vulnerable to adverse pharmacological events because of an increased risk of drugs interactions due to polypharmacotherapy and because of geriatric frailty [16]. This could be particularly the case of statins in which polypharmacotherapy interactions could increase the occurrence of muscle weakness or cramp leading to lower functional capacity. However, in our study, as well as in those published previously [11, 17], older patients showed a statistically significant functional improvement confirming the important role of CR also in this population.

The second most important finding to discuss is the sex implication [18]. In fact, females seemed to present lower functional improvement after CR. Nevertheless, as also founded in previous studies [5, 6, 9, 19], even female subjects increased appropriately their exercise capacity after CR course. Many reasons could explain these results. First of all, sex differences in diagnosis and treatment have been described. Women have smaller coronary arteries and less plaque burden but more apparent stenosis that is related to differences in remodelling [18], they present also a higher prevalence of spontaneous coronary dissection and myocardial infarction with no obstructive coronary atherosclerosis [20]. Women often present atypical symptoms, experience a smaller increase in cardiac enzymes and their CV risk is underestimated by traditional risk models resulting in diagnosis and treatment delays, and in higher rates of worse outcomes [21]. On the same issue, also personality traits and social roles traditionally ascribed to women could help explaining longer diagnosis and treatment delays in women [22]. Finally, women present also procedural technical

aspects (such as an higher rate of radial artery spasm) that could leads to an increased risk of complications (access site bleeding and contrast induced nephropathy) and receive less frequently guideline-suggested treatments in comparison with men [21, 23].

Moreover, women low adherence to CR programs is a very important issue that may interfere with the overall functional improvement. It is widely known that men are more adherent to CR programs and that recruitment for women is often significantly delayed [24]. For women, the barriers to CR participation are multiple and complex and possible solutions such as community and home-based physical activity and women-only cardiac rehabilitation should be offered and are actually under evaluation [25].

Another important determinant founded in our analysis was BMI that was associated with lower functional capacity during 6-MWT as also reported by some previous studies [5, 9]. We didn't collect discharge BMI and so we cannot relate it to the functional improvement, however, previous studies showed that obese patients who lost more than 5% of basal weight achieved a considerable improvement in exercise capacity, suggesting a possible association between the amount of weight loss and improvement in exercise capacity [9]. This result seems to suggest that an important effort to help patients reaching normal weight could be repaid by an increase in functional improvement. We must also say that weight loss often is a process longer than CR period and it is possible that what patients learn during CR could lead to further gain after CR itself.

In our study lower baseline HR was associated with higher functional capacity both before and after CR. Our findings are discordant with a previous study in which patients who initially showed evidence of the poorest state of fitness, with high rest HR, achieved a greater improvement after CR [26]. With regard to this, it is important to underline that HR value is strongly dependent on assumption of  $\beta$ -blockers. In our study all the patients took this drug class (principally bisoprolol) in order to reach a resting HR of 50–60 bpm. Patients with lower basal HR are those who better tolerate B-blockers and so who more benefit from their positive effects [27–29].

Previous studies also found that, despite a significant improvement of quality of life, weight loss and CV risk factors, diabetic subjects showed a significantly lower improvement in exercise capacity than non-diabetic subjects [10, 30]. We found that presence of DM and blood glucose values were associated with lower exercise capacity during 6-MWT and lower functional improvement after CR while these results were not confirmed at the multivariate analysis. However, DM prevalence in our population was low (16%) and this could be the reason why significant association was not found.

Finally, also anemia and hemoglobin level at baseline may have a relevant impact on functional capacity. Unfortunately,

we were not able to collect hemoglobin level in our patients and so to test its association with functional improvement. However, it certainly have a role in ACS patients prognosis and their functional status. In fact, a drop in hemoglobin level (even in the absence of significant bleeding, have been identify as an independent predictor of 1-year mortality [31]. Furthermore, anemia was found to be very prevalent (75.2% of the population) in cardiac rehabilitation patients and to be related to their functional capacity [32, 33]

Another point of our study that needs to be discuss, i.e the confirmation of the efficacy regarding functional improvement and the optimization of cardiovascular risk factor (lipid profile, BP and HR) as well as improvement in LVEF. Besides the well-known effect of physical exercise [34], these improvement can be interpreted as the reflection of the efficacy of other aspects of the CR program such as therapeutic optimization, risk factors information, food education and promotion of a healthy lifestyle.

Our paper presents some limitations. Firstly, the low number of enrolled patients and the single-centre design of our study could limit the generalizability of the study. Furthermore, some subgroups (i.e. females, obese patients, diabetics) presented a low number of subjects. This sample size could limit our power to detect important associations or findings. Regarding obese patients, we did not registered weight change during CR, thus limiting our possibility to understand if subjects that lost weight had the greater gain in functional capacity. However, as already stated, weight loss is often a process longer than CR period. Furthermore, we did not collect HR during stress test or CR, limiting our power to detect if also this variable (i.e. the dynamic HR response to exercise) could be a significant predictor of functional capacity and improvement. Finally, although six-minute walk test is frequently used in cardiac rehabilitation [35], most of the studies concerning patients with coronary artery disease used other tools to measure exercise capacity and functional improvement, such as Metabolic Equivalents (METs) [7, 10, 13, 36] and maximum oxygen consumption ( $VO_{2max}$ ) [11, 19]; instead, in other types of cardiological populations, such as patients with heart failure, functional capacity is typically estimated by the distance travelled during a walking test [37]. It is easy to understand that the determination and the evaluation of the same functional parameter could lead to difficult comparisons and interpretations when using different tools.

## 5 Conclusions

In conclusion, our study showed that the determinants of exercise capacity were age, BMI and HR, whereas determinants of functional improvement in patients undergoing CR were age, sex and BMI. Therefore, determinants of functional improvement are not

cardiological variables; they are intrinsic factors, both modifiable factors (BMI) and non-modifiable factors (age and sex).

These results suggest that a diversified or an intensified CR should be programmed for elderly, females or obese patients. However, how this could be translated into clinical practice is a matter of debate and focused studies are needed to answer these questions.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s40292-021-00473-7>.

## Declarations

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**Conflict of interest** The authors declares that there is no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of the Institution involved.

**Consent to participate** All participants provided informed written consent after being informed of its nature and purpose.

**Consent for publication** Not applicable.

**Availability of data and materials** On request to corresponding author.

**Code availability** On request to corresponding author.

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