Universitat de Girona
Facultat de Medicina

LONG-TERM BENEFITS OF THE CARDIAC REHABILITATION PROGRAMME IN GIRONA

A three-year follow-up study

FINAL DEGREE PROJECT

Author: Elena Canal Garcia

Tutor: Dr. Marco Antonio Paz Bermejo

Department of Cardiology
Santa Caterina Hospital
Faculty of Medicine, January 2017

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ABSTRACT

Background: Cardiac rehabilitation (CR) is the most effective approach following a cardiovascular event as a secondary preventive strategy. It consists of a multidisciplinary approach to overall cardiovascular risk reduction. Evaluation of the patient's cardiovascular risk factor profile is a crucial part for the management of CR patients. There is strong evidence about the short-term benefits of CR programmes in the control of the cardiovascular risk factors (CVRF), reducing mortality and improving quality of life. However, the beneficial effect of CR programmes on the risk reduction is not clear longer term.

Objective: Our aim was to determine the long-term control of CVRF, after a 3-year follow-up period, in patients referred to the CR programme of Santa Caterina Hospital of Girona, after suffering an acute coronary syndrome (ACS).

Methods: A retrospective observational follow-up study was conducted on a cohort of 213 patients (mean age 56 years) referred to the CR programme of Santa Caterina Hospital following ACS, between 2008 and 2013. We evaluated the long-term control of CVRF and the occurrence of major adverse cardiac events (MACE) in a 3-year period of follow-up. The short-term control of CVRF was analysed and the demographic and clinical characteristics of patients were determined. A comparison depending on the length of the CR programme was also performed.

Results: Of the 213 patients included, long-term control of low-density lipoprotein cholesterol (LDL-c) blood levels (85.45mg/dL vs 86.27mg/dL, P=0.669) and tobacco consumption (14.85% vs 18.78%, P=0.293) was maintained from post-CR to year three, although both showed a trend towards deterioration. There was a significant increase in systolic blood pressure (BP) (124.58mmHg vs 128.76mmHg, P<0.001), glycosylated haemoglobin (HbA1C) in diabetic patients (6.52% vs 7.10%, P<0.001) and body mass index (BMI) (28.36kg/m^2 vs 29.41kg/m^2, P<0.001) from post-CR to year three. Short-term CVRF control was significantly improved after discharge from the CR unit for all CVRF analysed. The incidence of MACE at the end of the follow-up was 16.4% and the total death was 2.8%. An extended-length CR programme was reported in 19.25% of the study population. No significant differences in the CVRF control were found between standard-length and extended-length CR programme in all CVRF analysed.

Conclusion: The long-term control of CVRF after enrolment in a CR programme has a trend towards deterioration after 3 years of follow-up, which has been significant for systolic BP, HbA1C and BMI. Further studies might be advantageous to confirm our findings.

Keywords: ■Acute coronary syndrome ■Cardiovascular risk factors ■Cardiac rehabilitation ■Secondary prevention

ABBREVIATIONS

ACEI	Angiotensin-converting-enzyme inhibitor
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
ARBs	Angiotensin II receptor blockers
BMI	Body mass index
BP	Blood pressure
CABG	Coronary arteries bypass grafting
CEIC	Clinical and Ethical Investigation Committee
CHD	Coronary heart disease
CR	Cardiac rehabilitation
CVD	Cardiovascular disease
CVRF	Cardiovascular risk factors
EF	Ejection fraction
ESC	European Society of Cardiology
HbA1C	Glycosylated haemoglobin
LDL-c	Low-density lipoprotein cholesterol
MACE	Major adverse cardiac events
NSTEMI	Non-ST elevation myocardial infarction
SCORE	Systematic coronary risk evaluation
SEC	Sociedad Española de Cardiología
STEMI	ST elevation myocardial infarction
UA	Unstable angina

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1. INTRODUCTION

1.1 Cardiovascular disease overview

Cardiovascular disease (CVD) is the leading cause of mortality and morbidity in developed countries, generating 31% of all deaths around the world (1). 17.5 million people die every year of CVD, with 80% caused by acute myocardial infarction (AMI) and stroke. This represents a major economic and resource burden on public health systems (2). In Europe, CVD causes a total of 4.5 million deaths per year (3). The most recent data from cardiovascular mortality in Spain shows that 29.66% of all deaths are related to CVD, representing 53.581 men and 63.812 women deaths in 2014. In Catalonia cardiovascular deaths represent a 27.61% of total deaths and in the province of Girona, there were 488 deaths linked to CVD (4).

Coronary heart disease (CHD) is a group of diseases which consist of a disorder of the heart and blood vessels most frequently associated to atherosclerosis (5). It is the most frequent form within the group of CVD and is a major cause of illness and death, including stable angina and acute coronary syndrome (ACS). Stable angina is a chronic status which develops during the same level of exertion and resolves at rest (6). Differently, ACS refers to a range of conditions associated with sudden, reduced blood flow to the heart. Three categories of ACS may be encountered: non ST-segment elevation myocardial infarction (NSTEMI), persistent ST-segment elevation myocardial infarction (STEMI) or unstable angina (UA). These categories are based on the electrocardiogram and biomarkers findings (7). The main difference lies in acute total coronary occlusion being present in STEMI cases but not in NSTEMI/UA, where the occlusion is partial or transitory (8).

The mortality rate from CVD is progressively decreasing, due to an improved management of ACS and a better control of the cardiovascular risk factors (CVRF) in the general population. However, increased longevity and advances in medical treatment have led to a progressive ageing of the population and to an increase of the prevalence of CVD. According to the *World Heart Federation*, there will be 23 million-deaths per year in 2030 caused directly by CVD (9). Given the high mortality and morbidity, it is important to recognize the early manifestations of the CHD. Unfortunately, AMI is the most frequent first manifestation of CHD. AMI is defined as the consequence of a blockage in the coronary arteries caused by a rupture of multifactorial fatty deposits on the inner walls of the blood vessels that supply the heart. The heart muscle loses its blood supply leading to necrosis of myocardial tissue and, thus, generating akinetic heart walls (10,11)**.**

1.2 Cardiovascular risk factors

CVD is generally due to a combination of multiple CVRF. These are defined as a measurable characteristic associated with increased disease frequency and they are a significant independent predictor of the risk of presenting the disease (12). The description of the natural history of CVD is shown in Figure 1. It has long been known that CVRF tend to cluster in individuals. Clustering of CVRF is particularly relevant when they tend to interact such that their combined adverse effect is not only greater than a summation of the individual components, but usually multiplicative (13).

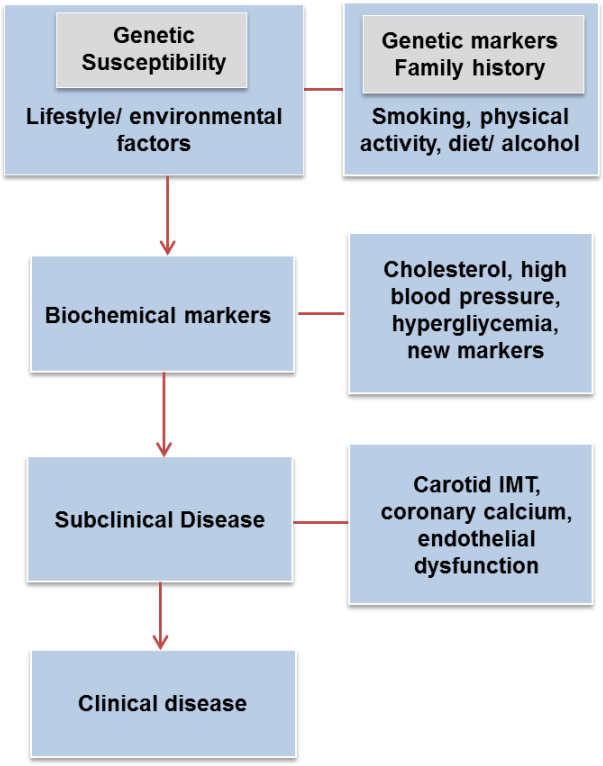

Figure 1 - Natural history of CVD. Adapted from O'Donnell et al (12).

The influence of CVRF in patients determines a probability of suffering from a CVD. Estimation of the patient's total risk of CVD is fundamental for the approach to prevention strategies. Risk stratification may help in management of decisions and in avoid both under or overtreatment. The higher the risk, the more intense the action should be. The risk categories are shown in Table 1. Apparently, absolute risk reduction is larger in those individuals at higher baseline risk. The main tool of primary cardiovascular risk stratification is the systematic coronary risk evaluation (SCORE) system. It has been developed to estimate an individual's 10-year risk of fatal CVD, in the European population. Systematic cardiovascular risk assessment is recommended in individuals at increased cardiovascular risk (family history of premature CVD, familial hyperlipidaemia, major CVRF or comorbidities increasing cardiovascular risk) every five years (14).

TABLE 1. Risk categories		
Low-risk	-	SCORE<1%
Moderate-risk	-	SCORE 1-5%
High-risk	-	Markedly elevated single risk factors, in particular cholesterol >310mg/dL or BP >180/110 mmHg.
	-	Most other people with diabetes mellitus.
	-	Moderate chronic kidney disease (GF 30-59mL/min)
	-	SCORE 5-10%
Very high-risk	-	Documented clinical CVD includes previous AMI, ACS, coronary revascularization, stroke, transient ischemic attack, aortic aneurysm and peripheral artery disease.
	-	Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound.
	-	Diabetes mellitus with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolemia or hypertension.
	-	Severe chronic kidney disease (GF<30 mL/min).
	-	SCORE >10%

Table 1 - Adapted from ESC Guidelines of CVD prevention in clinical practice 2016 (14).

**AMI: acute myocardial infarction; ACS: acute coronary syndrome; BP: blood pressure; CVD: cardiovascular disease; GF: glomerular filtration; SCORE: systematic coronary risk evaluation*

CVRF are divided into two broad categories: traditional CVRF and emerging CVRF. Emerging risk factors have been recently identified in an effort to improve risk assessment for CHD. Those are homocysteine, C-reactive protein, thrombophilia, heart rate, psychosocial factors, obstructive sleep apnoea syndrome and nutritional factors (low vitamin D levels). Nevertheless, until now there is not strong evidence about the clinical relevance in the association of these emergent factors and CHD. Contrarily, traditional CVRF are strongly linked to CHD and extremely frequent in the general population. They can be classified according its suitability to be treated, controlled or changed in potentially modifiable or non-modifiable. Preventive strategies are developed to improve the targets of modifiable CVRF. Hence, our study will particularly focus in the control of the modifiable CVRF. A brief description of the main traditional CVRF is provided below.

Modifiable CVRF:

- Smoking: Cigarette smoking is directly associated with CVD for current smokers. There are 1.000 millions of cigarette smokers worldwide. Despite the prevalence of smoking has decreased slightly in men, it has increased in women during the last decade (12).
- High blood pressure (BP): hypertension has been widely studied and associated with CVD. Framingham and other epidemiological studies, demonstrated that high BP has an independent positive association with CVD. The prevalence of hypertension in the adult population in Girona is estimated to be around 34% (12).

- Being overweight: Obesity is a chronic metabolic disorder directly associated with multiple comorbidities and an independent risk factor for all-cause mortality and cardiovascular mortality (12). It is rapidly approaching tobacco as the leading cause of preventable morbidity and mortality. Mediterranean diet reduces the incidence of major adverse cardiac events (MACE) (15).
- Physical inactivity: The relative risk of death from CHD for sedentary population is 1.9 (1.6-2.2, 95% confidence interval). 23% of general population are sedentary on the developed countries (3).
- Hyperlipidaemia: Low-density lipoprotein cholesterol (LDL-c) was < 70 mg/dL in only 26% of patients after ACS (16). In Girona, the trends in the proportion of total cholesterol, LDL-c and high-density lipoprotein cholesterol during the last 20 years, has fallen at the expense of increased optimal medical treatment (12).
- Diabetes mellitus is associated with a 3-fold increase in the likelihood of developing CVD (3). The prevalence of diabetes mellitus in Spain is 8% in women and 12% in men and seems to be stable (12).

Non-modifiable CVRF:

- Age: CVD becomes increasingly common with advancing age (1).
- Gender: strong male predominance of AMI is present in all age groups. Once past the menopause, women's risk is similar to the men's risk.
- Family history of heart disease: it increases the cardiovascular risk if first-degree blood relative has had CVD before 55 years old for a male relative or 65 years old for a female relative (1).
- Genetic factor: genetic and lifestyle factors have been recently found to be independently associated with susceptibility to CHD. Among patients at high genetic risk, a favourable lifestyle is associated with nearly 50% lower relative risk of CHD than it is an unfavourable lifestyle (17).
- Ethnic background: Ethnicity should be considered in CVD risk assessment. Cardiovascular risk varies considerably between immigrant groups. South Asians and sub-Saharan Africans have higher risk, while Chinese and South Americans have a lower risk (12).

Given the above, many factors impact on the likelihood of an individual suffering a cardiovascular event. The positive take on the knowledge of CVRF in determining CVD is that most cardiovascular events are preventable (18). This makes them particularly suitable for prevention strategies. Among all CVRF, smoking, hyperlipidaemia, hypertension, overweight and diabetes are the most relevant. Thus, public health policy should be aimed towards reinforcing prevention as much as achievable, focusing in the most important risk factors.

It is essential to adopt effective preventive strategies, with adequate awareness of CVRF, as they represent an important step toward halt disease progression and reduce CV mortality (19,20). In Section 1.3 an analysis of cardiac rehabilitation (CR) as the main prevention strategy follows.

The multifactorial nature of CVD and the interactions between risk factors mean that is difficult to make an intuitive assessment of an individual's future risk of disease. This has led to the development of international guidelines on the prevention of CVD to guide prevention strategies. The European Society of Cardiology (ESC) recommends the goals for modifiable CVRF. The main target levels are shown in Table 2.

TABLE 2. Risk factors goals	
Smoking	No exposure to tobacco in any form
BP	<140/90 mmHg
Body Weight	BMI 20-24.99 kg/m^2
Diabetes mellitus	HbA1C <7%
Lipids (LDL-c)	Very high risk: <70 mg/dL or a reduction of at least 50% if the baseline is between 70 and 135 mg/dL High risk: <100 mg/dL or a reduction of at least 50% if the baseline is between 100 and 200 mg/dL Low to moderate risk: <115 mg/dL
Physical activity	At least 150 minutes a week of moderate aerobic physical activity (30 minutes for 5 day/week) or 75 minutes a week of vigorous aerobic physical activity (15 minutes for 5 days/week) or a combination thereof.
Diet	Low in saturated fat with a focus on wholegrain products, vegetables, fruit and fish

Table 2 - Adapted from ESC Guidelines of CVD prevention in clinical practice 2016 (14).

**BMI: body mass index; BP: blood pressure; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol.*

Nonetheless, according to EUROASPIRE IV results in Europe, a large majority of CVD patients do not achieve the guideline standards for secondary prevention. Consequently, there is a high prevalence of persistent smoking; unhealthy diets and physical inactivity, and thus, most patients are overweight or obese with a high prevalence of diabetes (21). After all, the control of CVRF is not satisfactory even with high reported use of medications. A better fulfilment of therapeutic guidelines to treat CVRF can prevent the appearance or progression of CVD (22). Minor changes in only seven health indicators (diet, physical activity, body mass index (BMI), tobacco consumption, BP, LDL-c and glycosylated haemoglobin (HbA1C)) could induce dramatic reductions in cardiovascular risk of up to 93% (23).

1.3 Prevention: Cardiac rehabilitation programmes

CR programmes are defined as integral to comprehensive interventions designed to promote secondary prevention and to enhance quality of life among patients after a cardiac event. Historically, patients with ACS were advised to observe 6 weeks of bed rest. Chair therapy was introduced in the 1940s (24). In the early 1950s, a very short daily walk of 3 to 5 minutes was allowed 4 weeks after the ACS. Gradually, it was recognized that early ambulation prevented many of the complications of bed rest, and that it did not increase the risk. Over the past 2 decades, CR programmes after a diagnosis of an ACS, have gradually evolved from an exercise-based intervention into a comprehensive, professional lifestyle, behavioural interventions as detailed below. Nowadays, CR has appeared to be the most effective approach following a cardiovascular event as secondary preventive strategy to manage CVD, associated with a reduction in both cardiac mortality and total mortality (25–27).

CR is a multidisciplinary approach, which involves regular aerobic exercise combined with interventions for lifestyle changes such as education and health empowerment, nutritional counselling, behavioural strategies and psychosocial input focusing on health promotion. The purpose is to ensure the patient's best possible physical and psychosocial conditions, and thus, to modify permanently the individual behaviour. From all CR components, as seen in Figure 2, physical exercise remains the key intervention, as is the most scientifically proven (28,29). However, behaviour changes alone reduce >50% of cardiac mortality, morbidity and improves the targets of CVRF with a significant decrease in total cholesterol, systolic BP and active tobacco consumption (30).

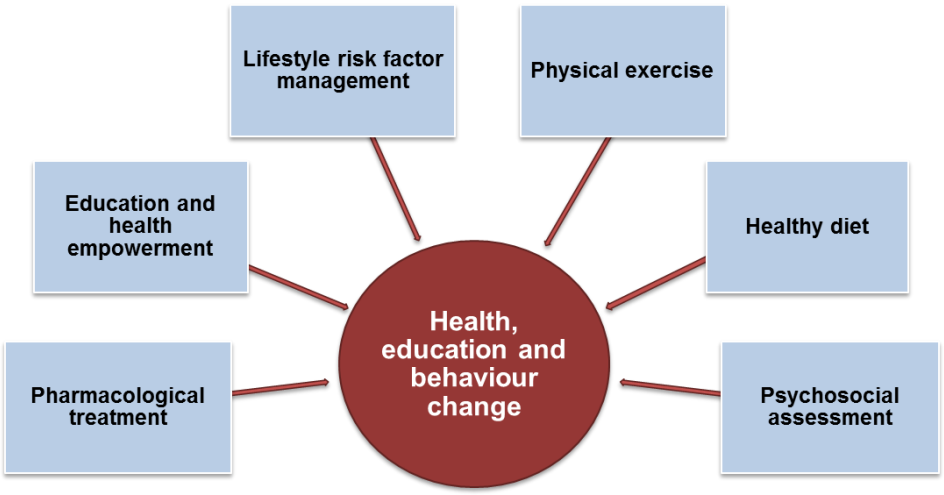

Figure 2 – Components of CR Programmes

CR has well-documented effects on symptoms reduction, improving functional capacity (physical training, psychological intervention and social integration) and modifying lifestyle behaviours (smoking cessation, diet, physical activity, medical risk factor management and psychosocial health) (31). CR also reduces hospital admissions as well as improves the quality of life. These results appear to be consistent across patients and intervention types. All those benefits are directly attributed to physiological favourable effects of exercise training on risk factors, behaviour and mood (32,33). For all its benefits, CR has been recently given a Class I recommendation from the American Heart Association, the American College of Cardiology and the ESC. The levels of evidence of CR programmes are shown in Table 3 (34–36).

TABLE 3. Levels of evidence of CR	
IA	Participation in a CR programme for patients hospitalized for an acute coronary event or revascularization, and for patients with heart failure, is recommended to improve patient outcomes.
IA	Prevention strategies are recommended in CVD patients, including lifestyle changes, risk factor management and pharmacological optimization, after an acute event before hospital discharge to lower risk of mortality and morbidity.
IB	Preventive programmes for therapy optimisation, adherence and risk factor management are recommended for stable patients with CVD to reduce disease recurrence.

Table 3 – Modified from ESC Guidelines of CVD prevention in clinical practice 2016 (14).
**CR: cardiac rehabilitation; CVD: cardiovascular disease.*

Although CR encompasses interventions for several heart diseases, it is mainly performed in CHD patients, especially in survivors of an AMI. At present, the gained experience in CHD has allowed extending CR to other forms of heart diseases used as an adjuvant therapy. The indications and contraindications of CR programmes are shown in Table 4 (36).

TABLE 4. Indications of CR programmes
- Patients with ACS, including STEMI, NSTEMI and UA, or patients undergoing reperfusion (coronary artery bypass surgery or percutaneous coronary intervention). Confirmed exertional angina. - Patients with newly diagnosed chronic heart failure and chronic heart failure with a step change in clinical presentation. Patients with heart transplant and ventricular assist device. - Patients who have undergone surgery for implantation of intra-cardiac defibrillator or cardiac resynchronisation therapy for reasons other than ACS and heart failure.
Contraindications of CR programmes
- Unstable heart disease. Aortic dissection. - Severe aortic stenosis with a sever obstruction in the left ventricle outflow tract. - Severe physical disability. Psychiatric illness.

*Table 4 - Modified from ESC Guidelines of CVD prevention in clinical practice 2016 (14). *ACS: acute coronary syndrome; CR: cardiac rehabilitation; NSTEMI: non-ST elevation myocardial infarction; STEMI: ST elevation myocardial infarction; UA: unstable angina.*

The core components of CR programmes have been standardized, but structure, length and type of the programme offered differs widely by country, affected by national guidelines and standards, legislation and economic factors. Standard CR programmes are hospital-based programmes supervised by the CR team. It is a multidisciplinary team composed by a cardiologist, a clinical nurse specialist, a physiotherapist, a psychologist, a clinical nutritionist and a social worker. It is essential that all CR staff have appropriate training and skills to practice within their scope and respect the other disciplines involved in providing comprehensive CR. Moreover, the CR team should actively link with the general practitioner and nurses to create a long-term approach to CVD management.

Standard CR programmes present a serial of phases that determine the structure and location of CR centres. They are shown in Figure 3. In our local area of Santa Caterina Hospital in Girona, the structure of the standard CR programme is composed by the following time frames:

- Phase I (in-hospital): From the cardiac event until hospital predischarge. First educational talks by the nursing staff regarding the illness, analysing behavioural habits, focusing on the weaker patterns are accomplished.

- Phase II (ambulatory): From hospital discharge until 2-4 weeks, the patient has to initiate the patterns of new healthy lifestyle. A psychologist visits the patient initiating an assessment of the follow up.

- Phase III (CR centre): After one month of discharge, the cardiologist visits the patient on the CR centre to perform an initial stress test. The stress test consists of walking on a treadmill using the Bruce programme, increasing the speed and slope every 3 minutes in a total of 15 minutes. The initial stress test serves to filter enrolments. Patients with ischemia and low exercise levels are excluded and indicated for coronary angiography. Depending on the results of this test and the clinical evaluation, the patient is accepted to CR centre. The CR programme consists of exercise-based one-hour supervised sessions 3 times a week, over a period of 8 to 12 weeks. Each session, patients perform individualised physical training, including aerobic training on mats or an exercise bicycle.

  CR programme also includes a psychological programme focusing in behaviour modification techniques, group therapy and relaxation sessions. Educational program is based on modifying lifestyle and controlling CVRF. Return to work counselling is accomplished during this phase. All activities are under-supervision by the CR team. At the end of the 12th week, another stress test is repeated to evaluate the results and the patient is discharge from the CR centre.

- Phase IV (maintenance): For the rest of patient's life. It consists of maintaining the healthy habits learned during the previous phases with follow-up by the general practitioner and the cardiologist. Patients are advised to continue taking exercise individually or in a gym following specific training recommendations.

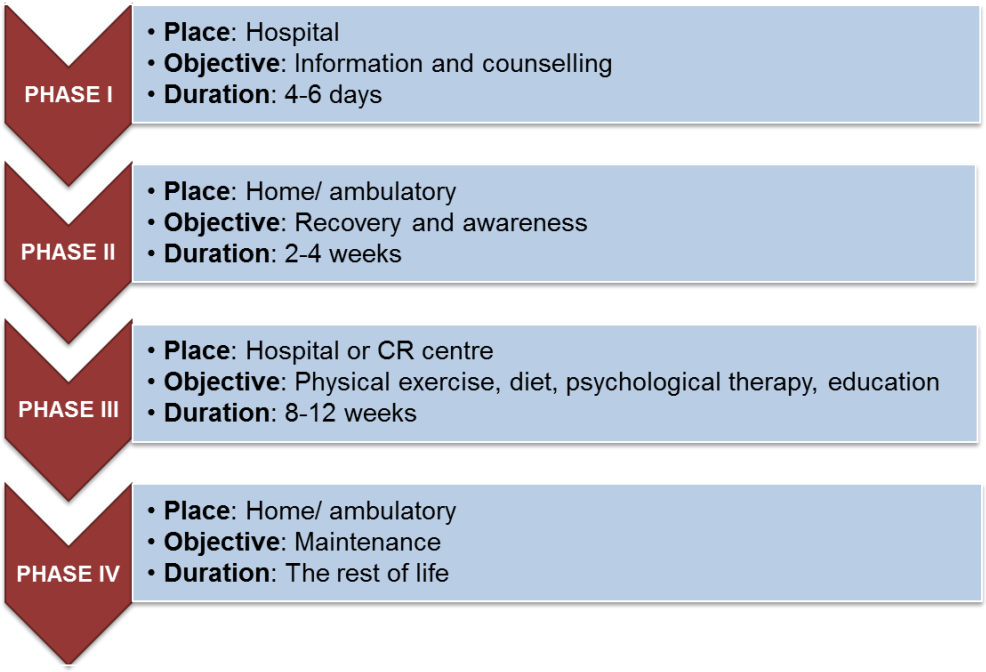

Figure 3 – Phases of a standard hospital-based CR programme

The early implementation of CR programmes has been shown to be both safe and feasible. Complications during the rehabilitation process are very uncommon. Muscle injuries, angina or cardiac arrhythmias are described as complications, but rarely pose a major problem.

1.3.1 Cost-effectiveness and participation rates

Besides the improvement in survival, CR programmes promote better quality of life, functional status and support early return to work. Thus, hospital-based CR programmes are efficient. Several factors, including the target population's age, gender, baseline CVRF, cost of drugs and other interventions, can modify the cost-effectiveness of CR programmes (37). Other elements such as comorbidities, self-efficacy, adherence, and attitude toward CR may also affect. These factors influence the results in cost-effectiveness amongst countries, which presents significant variations between them. In 2009, costs related to CVD represented 9% of the total healthcare expenditure across the European Union. Thus, CVD assume a considerable economic burden to society and cost-effective preventive measures are necessary (14).

Despite robust evidence of clinical and effectiveness of CR programmes, their implementation after ACS or revascularisation remains suboptimal, with low participation rates, estimated at 10% over recent decades (38). Most CHD patients are discharged from hospital without CR being recommended. Poor uptake has been attributed to several factors such as a low number of CR centres and a lack of access to the programme due to transport difficulties, work schedules, social commitments or even lack of perceived need. The underuse is partly due to the physicians' reluctance to refer small percentages of patients, particularly women, elderly population, ethnic minorities and lower socioeconomic classes (39). Adherence to CR programmes is also affected by factors such as psychological wellbeing, geographical location and a dislike of group based rehabilitation sessions. Along these lines, endorsement CR programmes in patients after ACS has become a challenge for the clinicians. This challenge has led to the development of a large and diverse array of alternative CR programmes (40).

According to the European Cardiac Rehabilitation Inventory Survey, only a few years ago, Spain was the European country with the fewest CR centres and activity (41). Most recent data has informed of an increase in the number of CR units, most of which account for tertiary hospitals in Madrid, Catalonia and Andalusia. In 2014, 115 CR centres implemented CR programmes. However, participation rates still remain very low, with 9% of patients with ACS being enrolled in CR (42).

Nowadays, hospital-based programmes are the dominant strategy representing 74% of CR programmes in Spain. The tendency reveals that both the number of patients with access to CR and the number of CR units will increase notably in the following years, according to the American registry of CR units (43).

1.3.2 Alternative models

Over the recent years, CR has evolved from a standard hospital-based approach to a mixed hospital-home monitoring strategy or a home-based approach involving telephone support (44). Home-based CR programmes for low-risk patients have been recommended, because they are equally effective when compared with traditional hospital-based CR programmes, and they improve the adherence, involving the same costs (45). In the same line, adherence of CR programmes is greater when less number of sessions are performed (46). Both hospital- and home-based CR programmes are more effective compared to no CR. Therefore, the choice of the mode of delivery should be left to patients and health professionals (47).

Other strategies like nurse-coordinated care programmes compared to usual CR programmes have demonstrated an improvement in the control of CVRF, leading to fewer readmissions and a reduction of mortality. Nurse is a useful link between the discharge and the ambulatory follow-up in order to maintain a better control of CVRF (48). Similarly, family-centred approach led to healthier lifestyle changes with more control of CVRF in patients and their partners compared with standard CP programme.

The new technologies will have a key role in alternative models linking between preventive health consultations and CR programmes. Telerehabilitation is promising but the evidence is still scarce (49). Nonetheless, promising results have been found with remote monitoring shirts equipped with monitoring and support software and even smart phone-based home monitoring (50). Multifactorial individualized telehealth, internet-based CR programmes and telehealth focused on exercise or on recovery are other examples of alternative models.

1.3.3 Long-term benefits

It is well recognised that current CR programmes achieve an optimal control of CVRF (smoking, hypertension, hyperlipidaemia, diabetes mellitus type 2 and overweight) in a short-term period following ACS (less than one year follow-up) (14). In terms of long-term benefits, the role of CR programmes in maintaining the control of those CVRF is not clear and there is only few evidence (51). Some authors have found satisfactory adherence rates and improved outcomes, not only at the end of the programme but also maintained along the years (52,53). They found CR programmes to be effective in decreasing the risk of several important cardiovascular outcomes, and, although the effect is small, it is maintained along years (54). Other authors have concluded an initial improvement of the outcomes, but some deterioration in the CVRF control through years (55,56). One 5-year follow-up study showed that tobacco consumption and cholesterol benefits were maintained at long-term, probably due to follow-up by general practitioners. Worse results were observed regarding systolic BP, BMI and physical exercise (57).

Given that CHD is a progressive chronic illness, a long-term evaluation is required to determine the long-term beneficial effects of CR programmes on mortality, morbidity and the level of CVRF control. Presumably, the benefits of CR programmes are mainly due to the healthy lifestyle habits that patients learn while they are undergoing the CR programme. If the new healthy lifestyle habits are maintained during the first year post-ACS, the CVRF control is likely to be maintained in the long-term (51). To all appearances, it would be interesting that after CR programme phase III concludes, patients continue with refresher sessions of rehabilitation on a continuous follow-up.

In Girona, a hospital-based CR programme is performed since 2008 at the Hospital of Santa Caterina involving patients, mostly after ACS. This study wants to contribute relevant information about the benefits in the long-term control of the CVRF among cardiac patients. The type of CR unit in Santa Caterina Hospital is a standard CR programme, so the data obtained from this study could be applied to the same type of units of CR in Spain. Moreover, this study aims to give knowledge about how successful is the CR programme of Girona.

2. JUSTIFICATION

CHD has a markedly high prevalence and represents a substantial impact on mortality and morbidity in developed countries. It corresponds to a health problem of considerable magnitude relative to the general population. With increasing longevity more people suffer from CHD, meaning that secondary prevention strategies have never been so important.

Over the last decade, CR programmes have proven its effectiveness in improving the control of CVRF, being beneficial for the physical and psychical condition of the patients and their quality of life. They have been established as a key strategy to reduce readmissions, re-infarctions, and thus, to achieve a drastic reduction in the mortality in patients after ACS. However, CR programmes are often forgotten by professionals and still remain the less used strategy despite all the evidence about the significant benefits they provide.

During the last years, evidence of the positive effect of CR programmes has increased, leaving almost no room for dispute in short-term studies. However, there is insufficient evidence to demonstrate if such effects are maintained longer term (51). Some studies have observed that the benefits of CR programmes are maintained, while others show that benefits tend to fade over the years. Duration and intensity of the intervention, in addition to the motivation of the participant, correlates with maintenance of the CR programme benefits. Therefore, some authors presume that the creation of CR units of permanent control of CVRF would avoid the relapses, maintaining the reduction of morbidity and mortality in the long term.

For all these reasons and taking into account the importance of prevention strategies, a 3-year follow-up study could provide new evidence on the control of CVRF in the long term after being enrolled in a hospital-based CR programme. Further knowledge in the long-term may be appropriate to influence how current CR programmes are run. Moreover, this study aims to provide knowledge of how secondary prevention is being achieved in Girona area. Likewise, a comparison in the length of the CR programme among patients could correlate with an improvement of the CVRF control. New evidence in this field could allow appreciating how best optimize the CR programmes prevention strategy in the near future.

3. HYPOTHESIS

Several suggestions related to the control of CVRF in patients after enrolment in a CR programme have been made, specifically for the CR unit of Girona's Health region.

It is suggested that patients enrolled in the CR programme of Santa Caterina Hospital after an ACS achieve behavioural and lifestyle changes, resulting in a better control of the CVRF in secondary prevention. The incidence of MACE during the period of follow-up should be low, considering the reported effectiveness of CR programmes in reducing mortality. However, it is believed that the control of the CVRF is not maintained over the years.

Furthermore, as duration and intensity of the intervention correlates with maintenance of the control of CVRF, it is believed that an extended-length CR programme in patients after ACS should be associated with better maintenance of the control of CVRF along years, in comparison with a standard-length CR programme.

4. OBJECTIVES

Main objective:

- To determine whether the control of the CVRF (tobacco consumption, hypertension, hyperlipidaemia, diabetes mellitus type 2 and overweight) is maintained at long term (after 3 years of discharge of the CR unit), among all patients referred to the hospital-based CR programme of Santa Caterina Hospital from Girona area, after suffering an ACS.

Secondary objectives:

- To assess the short-term benefits regarding CVRF control among all patients post-ACS referred to the hospital-based CR programme of Santa Caterina Hospital.
- To describe the demographic and clinical characteristics of the patients enrolled in the CR programme of Santa Caterina Hospital from the province of Girona, after suffering an ACS.
- To determine the incidence of MACE among all patients post-ACS referred to the hospital-based CR programme of Santa Caterina Hospital, after 3 years of follow-up.
- To ascertain the benefits of a voluntarily extended-length CR programme in comparison to the standard-length CR programme among all the patients enrolled in the CR programme of the Santa Caterina Hospital in Girona, after suffering an ACS.

5. METHODOLOGY

5.1 Study design

It is a descriptive observational retrospective study of a cohort composed of CR patients, with a 3-year period of follow-up.

For the last secondary objective, the study population has been divided in two cohorts, depending on the length of the CR programme.

5.2 Participants

The study population includes individuals referred to the hospital-based CR programme through the Cardiology unit at Santa Caterina Hospital of Girona, after suffering an ACS, between January 2008 and December 2013. A target population of 227 patients were referred to the CR unit during this period. According to inclusion and exclusion criteria, 213 patients were recruited in the retrospective analysis of Girona's health region.

5.3 Inclusion and exclusion criteria

Inclusion criteria:

- Patients enrolled in the hospital-based CR programme of Santa Caterina Hospital of Girona from January 2008 until December 2013.
- Patients diagnosed with ACS – including STEMI, NSTEMI and UA - admitted in the cardiology unit of Santa Caterina Hospital of Girona and Hospital Universitari Dr. Josep Trueta of Girona.
- Patients able to read the information paper and to provide written informed consent of the CR programme of the Santa Caterina Hospital.

Exclusion criteria:

- Patients enrolled in the hospital-based CR programme of Santa Caterina Hospital of Girona with a different diagnosis of heart disease: cardiovascular surgery, congestive heart failure, valvulopathy, etc.
- Data unavailable for a 3-year follow-up study ± 6 months.
- Patients with severe comorbidities or limitation for physical activity, and thus, inability to undergo CR programmes.
- Stress test with induced significative ischemia with low charge of exercise, arrhythmia induced with the exercise or hypotension response to this.
- Ventricular arrhythmias and other malignant arrhythmias.

5.4 Sampling method and sample power

A consecutive non-probabilistic sampling-method has been performed. Sample recruitment has consisted in collecting data of all patients that were enrolled in the CR unit of Santa Caterina Hospital after undergoing an ACS from January 2008 until December 2013, considering the inclusion and exclusion criteria.

Given the sample size of 213 subjects, accepting an alpha risk of 0.05 and considering it is a paired sample (matched pairs), the statistical power of the study population is 82.7% to recognize an effect size equal or more than 0.2 (based on Cohen interpretation). Likewise, the statistical power is 100% to recognize an effect size equal or more than 0.5. Sample power has been calculated with Gpower Version 3.1.9.2. (see appendix A).

5.5 Variables

5.5.1 Outcome variables

The outcome variables recorded in this study are the modifiable CVRF which include tobacco consumption, hypertension, hyperlipidaemia, overweight and diabetes mellitus type 2. According to ESC Guidelines of CVD prevention in clinical practice 2016, the optimal control for each risk factor has been defined (14). The description of the outcome variables is the following:

- **LDL-c:** it is measured in milligrams/decilitre (mg/dL). The variable has been analysed in two different ways:
    - LDL-c blood levels: continuous quantitative variable. It has been expressed with the arithmetic mean and the standard deviation.
    - Hyperlipidaemia control: dichotomous qualitative variable. The optimal control is defined when LDL-c <70 mg/dL and the non-optimal control is defined when LDL-c ≥70mg/dL. It has been expressed as an absolute value and a percentage.

  LDL-c has been obtained by retrospective review of computerized clinical charts, precisely from the records of previous blood tests which had been done by trained health professionals.

  Total cholesterol, high-density lipoprotein cholesterol and triglycerides were not recorded because of all the forms of cholesterol in the blood, the LDL-c is considered the most important form in determining risk of CVD.

- **Systolic BP:** it is measured in millimetres of mercury (mmHg). In order to decide which BP value we considered for the analysis, the systolic or the diastolic BP, a Pearson correlation was done in order to evaluate the correlation between both measures. Given that they have a high correlation (0.744), the variable BP is evaluated only through the systolic BP.

  The variable has been analysed in two different ways:

  - Systolic BP: continuous quantitative variable. It has been expressed with the arithmetic mean and the standard deviation.
  - Hypertension control: dichotomous qualitative variable. The optimal control is defined when systolic BP <140 mmHg and non-optimal control is defined when systolic BP ≥140 mmHg. It has been expressed as an absolute value and a percentage.

  Systolic BP has been obtained by retrospective review of computerized clinical charts, concretely from the physical examination. Ideally, BP should had been measured by trained practitioners using a manual sphygmomanometer and a stethoscope for auscultation, measured in the supine position after 10 minutes of rest in a quiet room at a room temperature of 22ºC.

- **BMI:** it is calculated through weight (kilograms) and height (metre^2) = kg/m^2. The variable has been analysed in two different ways:

  - BMI: continuous quantitative variable. It has been expressed with the arithmetic mean and the standard deviation.
  - Overweight control: dichotomous qualitative variable. The optimal control is defined when BMI is <25 kg/m^2, whereas BMI ≥25 kg/m^2 is defined as non-optimal control. It has been expressed as an absolute value and a percentage.

  BMI has been obtained by retrospective review of computerized clinical charts, concretely from the periodical physical examinations where weight and height were recorded by the general practitioner or the nurse.

- **HbA1C:** it is expressed by percentage (%) measured with the HbA1c blood levels. The variable has been analysed in two different ways:

  - HbA1C blood levels: continuous quantitative variable. It has been expressed with the arithmetic mean and the standard deviation.
  - Diabetes mellitus type 2 control: dichotomous qualitative variable. The optimal control is defined when HbA1C is <7% while non-optimal control is defined when HbA1C is ≥7%. It has been expressed as an absolute value and a percentage.

HbA1C has been determined by retrospective review of computerized clinical charts, precisely from the records of previous blood tests which had been done by trained health professionals.

- **Tobacco Consumption:** it is a dichotomous qualitative variable (smoker / non-smoker). The variable has been expressed as an absolute value and a percentage. It has been obtained by retrospective review of computerized clinical charts.

5.5.2 Secondary outcome variables

- MACE: Incidence of MACE during the 3-year period of follow-up. It is defined as the occurrence of the following events during the follow-up: ACS, need for revascularization by percutaneous intervention or coronary artery bypass grafting (CABG), stroke, cardiovascular death and/or sudden death.
  It is a dichotomous qualitative variable (yes/no). It has been expressed as an absolute value and a percentage. It has been obtained by retrospective review of computerized clinical charts.

- CVRF control: is the dependent variable corresponding to the last secondary objective which aims to compare the control of CVRF depending on the length of the CR programme. It is analysed stratified, equivalent to the previous explanation for the outcome variables (see section 5.5.1).

5.5.3 Covariates

Clinical and epidemiological characterization of patients enrolled in the CR programme has been performed. Their main baseline characteristics have been obtained from retrospective review of computerized clinical charts.

Sociodemographic variables:

- Age: continuous quantitative variable. It is defined in years. It had been collected at the moment of the ACS event. The age is important given that it is correlated with an increased probability of cardiac events. It has been expressed as an arithmetic mean and standard deviation.

- Gender: dichotomous qualitative variable (male/female). It has been expressed as an absolute value and a percentage. It is important because the CVRF are usually more present in men and they are more referred to CR programmes.

Clinical variables:

- Depression: dichotomous qualitative variable (yes/no). The mental status could modify the adherence to the CR programme. It has been expressed as an absolute value and a percentage.

- Type of ACS: Categorical qualitative variable (STEMI or NSTEMI/ UA). The type could imply different prognosis. It has been expressed as an absolute value and a percentage.

- Left ventricular ejection fraction (EF): Categorical qualitative variable (preserved >50%, mild 40-50%, moderate 30-39.99% or severe dysfunction <30%). Ventricular dysfunction is associated with worse prognosis. It has been expressed as an absolute value and a percentage.

Patient medical history: the following variables are dichotomous qualitative and have been expressed as an absolute value and a percentage.

- Tobacco consumption (smoker / non-smoker).
- Hypertension (yes/no). It is defined when BP >140/90 mmHg.
- Dyslipidaemia (yes/no). It is defined when LDL-c >70 mg/dL.
- Overweight (yes/no). It is defined when BMI ≥25kg/m^2.
- Obesity (yes/no). It is defined when BMI ≥30kg/m^2.
- Diabetes mellitus type 2 (yes/no). It is defined when HbA1C >7%.

Medical therapy after the ACS event: they have been expressed as an absolute value and a percentage.

- Aspirin: dichotomous qualitative (yes/no)
- P2Y12 inhibitors: categorical qualitative (clopidogrel / ticagrelor / prasugrel / no)
- β -blockers: dichotomous qualitative (yes/no)
- Angiotensin-converting-enzyme inhibitors (ACEI)/ Angiotensin II receptor blockers (ARBs): dichotomous qualitative (yes/no)
- Statins: dichotomous qualitative (yes/no)

5.5.4 Independent variable

Regarding the last secondary objective, the study population has been divided in two cohorts, depending on the length of the CR programme. Thus, an independent variable is defined:

- Length of the CR programme: It is a dichotomous qualitative variable (standard-length/extended-length). Standard-length CR programme in Santa Caterina Hospital consists of exercise-based one-hour supervised sessions 3 times a week, over a period of 8 to 12 weeks. The extended-length CR programme is an available option for patients enrolled in the CR unit who want to continue the programme when the standard phase ends. It has been obtained by retrospective review of the database of patients enrolled in the CR programme. It has been expressed as an absolute value.

5.6 Data collection and procedures

An electronic database has been created in order to collect the relevant data with *Microsoft Excel* ® informatics program (see appendix B). Once the Clinical and Ethical Investigation Committee (CEIC) of the Hospital Universitari Josep Trueta approved the project, data has been retrospectively registered in the database by assessment of the computerized clinical charts of the patients enrolled in the CR programme and by reviewing CR registration forms available. After data collection, a final review of the database has been done to ensure all participants were included in the study according to the inclusion and exclusion criteria. Homogeneity in data collection is ensured, as only one person has performed the collecting task. To maintain data anonymity and confidentiality, the database has been codified and an identification number has been created for each participant in the study. No telephone calls have been needed for database fulfilment.

The actual clinical charts are computerized in an informatics program (*SAP* program ®). The clinical chart is up-to-date in every medical visit. The multidisciplinary team of health professionals, who attend the patient, update the medical history, physical examinations, complementary tests, new events, etc. in the computerized informatics system. It is a reliable source of information of the evolution of the patients. Moreover, *SAP* program ® is according to the existing laws of patient confidentiality and data protection. The material used for the study was a laptop with access to *SAP* program ® and a laptop with database creator software tools (*Microsoft Excel* ®).

Data for risk factor analysis has been collected during three temporary periods:

- At the moment of the ACS event: clinical revision, an update of unhealthy habits (tobacco consumption), general measures (weight and systolic BP) and a blood test (LDL-c, HbA1C) were evaluated by the cardiologist before secondary prevention was implemented to the patient.

- After patients discharge from the CR unit: clinical revision, an update of unhealthy habits (tobacco consumption), general measures (weight and systolic BP) and a blood test (LDL-c, HbA1C) were evaluated by the cardiologist, general practitioner and nurse. With these items, the control of the CVRF (tobacco consumption, hypertension, hyperlipidaemia, diabetes mellitus type 2 and overweight) after the effects of being enrolled in the CR programme has been analysed.

- After a 3-year period of follow-up ± 6 months: the same measures were collected and the long-term control of the CVRF has been analysed.

Regarding the secondary objectives, during the 3-year period of follow-up, the incidence of MACE has been registered. Likewise, the baseline characteristics of the participants in the study have been collected. For the last secondary objective of the study, the population has been divided in two groups depending on the length of the programme: standard-length or extended-length. The extended-length CR programme is an option that CR unit of Santa Caterina Hospital gives, but with additional costs. Hence, not all subjects can afford it.

In regard to the follow-up period, we have considered that the most advantageous follow-up period for our study would be 3 years. A larger period would have reduced significantly our sample size, whereas a shorter period would not have been enough considering our main objective. To note, not all data was available exactly at the year three, so a period of ± 6 months has been accepted to record the measures.

6. STATISTICAL ANALYSIS

6.1 Descriptive analysis

The outcome variables LDL-c, systolic BP, BMI and HbA1C have been expressed in two different ways. First, they have been analysed as a continuous quantitative variable and, in a secondary analysis, as a dichotomous qualitative variable (optimal/non-optimal control). Tobacco consumption has been considered a dichotomous categorical variable (smoker/non-smoker). For quantitative variables, assuming they are normally distributed, data is expressed with the arithmetic mean, the standard deviation, the maximum and the minimum value. For qualitative values, data is given as absolute values and percentages.

Basal characteristics of the population have been described using absolute values and percentages for qualitative categorical variables. Those are gender, type of cardiac event, classification of left ventricular dysfunction, medical history and medical treatment. Quantitative basal characteristics of the population (age, BMI and EF) have been described using the arithmetic mean, the standard deviation, the maximum and the minimum value.

6.2 Bivariate analysis

The outcome variables LDL-c, systolic BP, BMI and HbA1C follow a normal distribution for paired data. A paired t-student test has been used for comparison quantitative continuous variables among pre-rehabilitation and post-rehabilitation, and among post-rehabilitation and year three. Chi-squared test (χ^2) and test of proportions have been used for comparison of the qualitative dichotomous variable (tobacco consumption) between pre-rehabilitation and post-rehabilitation, and for post-rehabilitation and year three.

An unpaired t-student test has been performed for comparison of each CVRF (continuous quantitative variables) between the two independent groups (standard-length vs extended-length, as dichotomous qualitative variable). χ^2 and test of proportions has been used to compare the incidence of MACE and tobacco consumption among both groups, since both variables are dichotomous qualitative.

A confidential interval of 95% has been used to ascertain in all different CVRF analysis. Those variables statistically significant have been considered when p value <0.05. The statistical analysis has been conducted using Statistical Package for Social Sciences (SPSS ®) for Windows V22 and STATA/IC13 ® programme.

7. RESULTS

The target population have been 227 patients referred to the CR programme of Hospital Santa Caterina from 2008 to 2013, with a mean follow-up of three years plus/minus six months. A total of 14 patients were excluded for different criteria: 6 patients were excluded given that they had not suffered a previous ACS, 3 patients due to them moved to another area and 5 patients due to loss of information during the follow-up. Finally, a total of 213 patients were included in our statistical analysis. The reasons can be seen summarized in a flowchart in Figure 4.

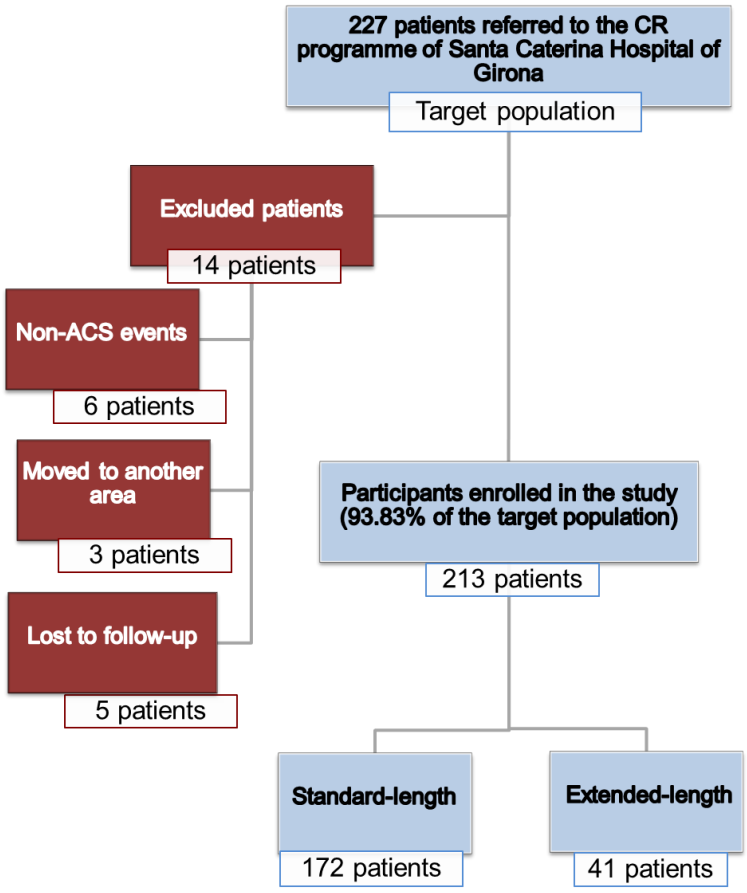

Figure 4 – Study flowchart

7.1 Demographic and clinical data

The baseline characteristics of the study population are shown in *Table 5*. In the study, mean age has been 56 years (range 26-75). The proportion of patients older than 65 years has been found to be the minority (19.7%), whereas males have been the majority of the population (86.9%). Concerning the ACS event, 128 patients have been enrolled in the programme following STEMI, and 66.2% subjects have been found to have a preserved ejection fraction. Risk factor profile assessment demonstrates that participants are majorly smokers (54.9%), with hyperlipidaemia (62.3%) and hypertension (54%).

A low rate of subjects have been found diabetic (17.8%) and depressive (13.6%). A total of 86.7% subjects reported a BMI >25 kg/m^2. All patients have been prescribed acetylsalicylic acid, and most of them have been prescribed statins (98.6%), β-blockers (93.4%), clopidogrel (85.9%) and ACEI/ARBs (65.7%).

TABLE 5. Baseline characteristics of the CR patients

Characteristic	Mean	Range	SD
Age (years)	55.85	26-75	9.45
BMI (Kg/m^2)	28.34	18.51-44.04	3.99
EF (%)	56.71	30-83	8.58
	N	**Percentage**	
Male	185	86.9%	
Female	28	13.1%	
<65 years	171	80.3%	
>65 years	42	19.7%	
STEMI	128	60.1%	
NSTEMI/UA	85	39.9%	
Preserved EF	141	66.2%	
Mild dysfunction	64	32.8%	
Moderate dysfunction	2	1%	
Sever dysfunction	0	0%	
Tobacco consumption	117	54.9%	
Hypertension	115	54.0%	
Hyperlipidaemia	132	62.3%	
Diabetes mellitus	38	17.8%	
Depression	29	13.6%	
Overweight	100	49.3%	
Obesity	76	37.4%	
Aspirin	213	100.0%	
Clopidogrel	183	85.9%	
Prasugrel	12	5.6%	
Ticagrelor	9	4.2%	
No P2Y12 inhibitor	9	4.2%	
β -blockers	198	93.4%	
ACEI/ ARBs	140	65.7%	
Statins	210	98.6%	

*Table 5 *ACEI: angiotensin-converting-enzyme inhibitor; ARBs: angiotensin II receptor blockers; BMI: body mass index; CR: cardiac rehabilitation; EF: ejection fraction; NSTEMI: non-ST elevation myocardial infarction; SD: standard deviation; STEMI: ST elevation myocardial infarction; UA: unstable angina.*

7.2 CVRF control data

The results of the different CVRF control have been evaluated separately. Detailed data is shown in Tables 6 - 8, and the CVRF control at the different time points during the follow-up is shown in Figure 5.

LDL-c

Mean LDL-c level was 132.58 mg/dL (range 33-249). The 98.1% of the study population were reported LDL-c levels ≥ 70 mg/dL at the cardiac event. Only 4 patients showed LDL-c levels < 70 mg/dL at the event.

After patients discharged from the CR unit, the mean LDL level decreased to 85.17 mg/dL (range 36-176), being as a result 64.3% subjects well controlled (n=137). Analysis of the results shows that improvement post CR achieves statistical significance (p<0.001). At the end of the 3-year period of follow-up, 57 subjects have been reported LDL-c levels < 70 mg/dL (27.5%), with a mean LDL-c level of 86.27 mg/dL (range 38-217). There has been no significant increase in the lipid levels between post CR programme and the 3-year period of follow-up (p=0.669).

Systolic BP

Mean systolic BP was 137.20 mmHg (range 90-180) at the moment of the ACS event. Hypertension was well controlled in 68.1% patients at that moment. After patients discharge from the CR unit, mean systolic BP was 124.58 mmHg (range 90-180) and the hypertension was well controlled in 87% of the patients. There was significant difference between pre and post CR programme (p<0.001), achieving an improvement in the control of hypertension risk factor. After the 3-year period of follow-up, the 87.1% of the study population have shown well-controlled hypertension. The mean has been 128.76 mmHg (range 82-172) and only 27 patients have not achieved the secondary prevention target. There have been significant increased levels of blood pressure between post CR programme and the 3-year follow-up (p=0.001).

BMI

Mean BMI at the moment of the ACS event was 29.42 kg/m^2 (range 20.52-45.60). Only 16.4% of the patients reported a BMI lower than 25 kg/m^2 (n=35). At the end of CR programme, the mean BMI was 28.36 kg/m^2 (range 18.51-44.04). 19.7% of the patients were reported a BMI lower than 25 kg/m^2 (n=42). Analysis of the results shows there has been significant reduction between pre and post CR programme (p<0.001). When the 3-year follow-up concluded, 18.4% of the study population has maintained a BMI lower than 25 kg/m^2. The mean BMI at this moment has been 29.41 kg/m^2 (range 19.49-44.43). There has been a significant increase of weight between post CR programme and 3-year follow-up (p=0.001).

HbA1C

Mean HbA1C level among diabetic patients was 8.95% (range 5.5-15.9). At the moment of ACS event, 59.5% diabetic patients were well controlled (n=25). At the end of the CR programme, 81.8% diabetic patients had the HbA1C on target (n=63). The mean HbA1C level was 6.52% (range 4.3-11.3) after the CR programme. Analysis of the results shows there was significant difference between pre and post CR programme (p<0.001).

At the end of the 3-year period of follow-up, 65.9% diabetic patients have been reported an on-target HbA1C level. The mean HbA1C level at this moment has been 7.10% (range 4.8-11.5). There has been a significant increase of HbA1C between post CR programme and 3-year follow-up (p=0.001)

Tobacco consumption

At the moment of the ACS event, 117 smokers were reported (55% of the study population). After patients discharge from the CR unit, 85.1% of the patients were not smokers (n=172). Analysis of the results shows there was significant reduction in the proportion of smokers post CR (p<0.001). 160 patients (81.22%) have been defined as non-smokers at the end of the 3-year period of follow-up. 7 patients have restarted smoking during the follow-up. There has been no significant difference between post CR programme and 3-year follow-up (p=0.293).

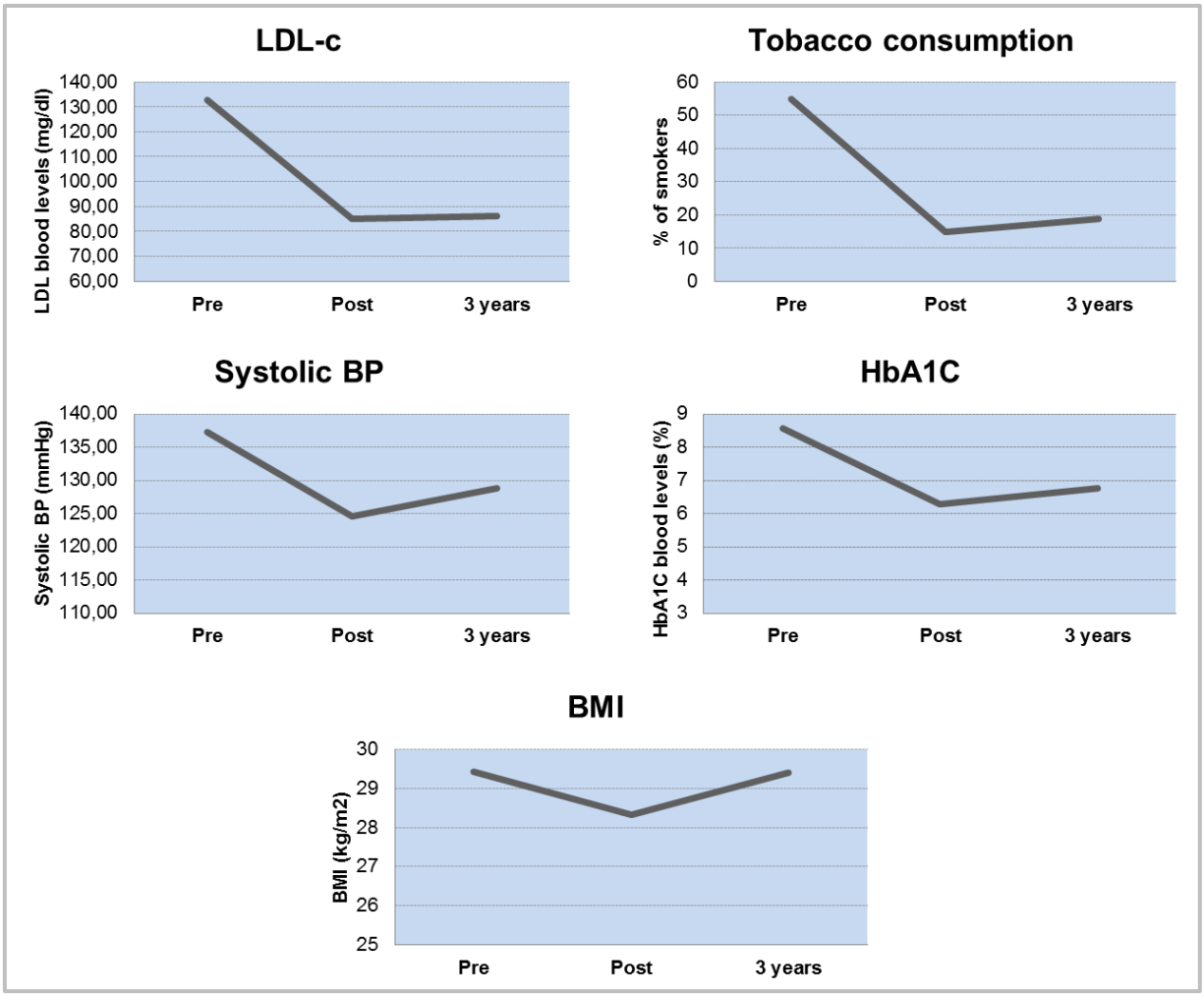

*Figure 5 - CVRF control at three time points. *BMI: body mass index; BP: blood pressure; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; Pre: previous; Post: Posterior.*

TABLE 6. CVRF repeated measures across three time points					
TOTAL	**Mean**	**Max**	**Min**	**SD**	**N**
LDL-c Pre	132.58	249	33	36.23	205
LDL-c Post	85.17	176	36	26.22	204
LDL-c 3 years	86.27	217	38	27.86	200
Systolic BP Pre	137.20	180	90	13.96	213
Systolic BP Post	124.58	180	90	14.65	212
Systolic BP 3 years	128.76	172	82	13.62	207
BMI Pre	29.42	45.6	20.52	4.22	204
BMI Post	28.36	44.04	18.51	3.99	211
BMI 3 years	29.41	44.43	19.49	4.51	206
HbA1C Pre	8.95	15.9	5.5	2.66	42
HbA1C Post	6.52	11.3	4.3	1.34	89
HbA1C 3 years	7.10	11.5	4.8	1.53	90
	Yes (%)	**No** (%)	**Yes** (N)	**No** (N)	**N**
Tobacco Pre	55%	45%	117	96	213
Tobacco Post	14.85%	85.15%	30	172	202
Tobacco 3 years	18.78%	81.22%	37	160	197

*Table 6 *CVRF: cardiovascular risk factors; BMI: body mass index; BP: blood pressure; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; Pre: previous; Post: posterior; SD: standard deviation.*

TABLE 7. Comparison of pre CR and post CR programme			
ENTIRE SAMPLE (N=213)	**Pre** Mean (SD)	**Post** Mean (SD)	**P-value** Pre vs Post *paired-t student test*
LDL-c (N=196)	132.58(37.71)	85.17(26.14)	<0.001
Systolic BP (N=212)	137.20(13.96)	124.58(14.64)	<0.001
BMI (N=204)	29.42(4.22)	28.36 (4.03)	<0.001
HbA1C (N=60)	8.95 (2.61)	6.52 (1.34)	<0.001
Tobacco consumption (N=202)	**N (%)**	**N (%)**	**P-value** Pre vs Post *Chi-squared test*
Yes	117 (55%)	30 (14.85%)	
No	96 (45%)	172 (85.15%)	<0.001
Total	213	202	

*Table 7 *BMI: body mass index; BP: blood pressure; CR: cardiac rehabilitation; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; Pre: previous; Post: posterior; SD: standard deviation.*

TABLE 8. Comparison of post CR and the year 3 of the follow-up			
ENTIRE SAMPLE (N=213)	**Post** Mean (SD)	**3 years** Mean (SD)	**P-value** Post vs 3 years *paired-t student test*
LDL-c (N=194)	85.45(26.14)	86.27(28.08)	0.669
Systolic BP (N=212)	124.58(14.64)	128.76(13.62)	0.001
BMI (N=204)	28.36(4.03)	29.41(5.73)	0.001
HbA1C (N=60)	6.52 (1.34)	7.10 (1.53)	0.001
Tobacco consumption (N=202)	**N (%)**	**N (%)**	**P-value** Post vs 3 years *Chi-squared test*
Yes	30 (14.85%)	37 (18.78%)	
No	172 (85.15%)	160 (81.22%)	0.293
Total	202	197	

*Table 8 *BMI: body mass index; BP: blood pressure; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; SD: standard deviation; Post: posterior.*

7.3 MACE data

The incidence of MACE after 3 years of follow-up has been 16.4% (n=35). Among all the participants, 6 subjects died during the follow-up, representing 2.8% of the study population. Cardiovascular death represented the main cause of death. Nonfatal ACS has been found to occur in 13.6% (n=29).

7.4 Comparison of the standard-length and the extended-length CR programme regarding the CVRF control

A total of 41 subjects (19.25%) have been found to participate in an extended-length CR programme. The mean additional period has been 37 months (standard deviation 25.77). Baseline characteristics of both groups are detailed in Table 9. The statistical analysis of the results has shown there was no significant differences in all CVRF analysed between both groups. Comparison analysis is presented in Table 10.

TABLE 9. Comparison of the baseline characteristics of the patients depending on the length of the CR programme

	Standard-length			Extended-length		
Characteristic	**Mean**	**Range**	**SD**	**Mean**	**Range**	**SD**
Age (years)	55.16	26-74	9.49	58.61	32-75	9.03
BMI (Kg/m^2)	29.44	20.52-45.6	4.36	29.35	22.20-38.51	3.49
EF (%)	56.74	30-83	8.67	56.59	40-70	8.04
	N	**Percentage**		**N**	**Percentage**	
Male	147	87.0%		35	85.4%	
Female	22	13.0%		6	14.6%	
<65 years	138	81.2%		31	75.6%	
>65 years	32	18.8%		10	24.4%	
STEMI	100	58.8%		26	63.4%	
NSTEMI/UA	70	41.2%		15	36.6%	
Preserved EF	114	67.1%		29	70.73%	
Mild dysfunction	54	31.8%		12	29.27%	
Moderate dysfunction	2	1.2%		0	0%	
Sever dysfunction	0	0%		0	0%	
Tobacco consumption	100	58.8%		15	36.6%	
Hypertension	90	52.9%		23	56.1%	
Hyperlipidaemia	104	61.5%		26	65.0%	
Diabetes mellitus	31	18.5%		6	14.6%	
Depression	24	14.1%		4	9.8%	
Overweight	76	46.34%		24	58.5%	
Obesity	64	39.63%		14	34.1%	
Aspirin	170	100.0%		41	100%	
Clopidogrel	147	86.5%		35	85.4%	
Prasugrel	10	5.9%		1	2.4%	
Ticagrelor	5	2.9%		4	9.8%	
No P2Y12	8	4.7%		1	2.4%	
β -blockers	160	95.2%		35	85.4%	
ACEI/ ARBs	107	62.9%		31	75.6%	
Statins	168	98.8%		40	97.6%	

*Table 9 *ACEI: angiotensin-converting-enzyme inhibitor; ARBs: angiotensin II receptor blockers; BMI: body mass index; CR: cardiac rehabilitation; EF: ejection fraction; NSTEMI: non-ST elevation myocardial infarction; SD: standard deviation; STEMI: ST elevation myocardial infarction; UA: unstable angina.*

TABLE 10. Comparison of the standard-length and the extended-length CR programme regarding the CVRF control

Parameter	**Standard-length** (N = 172) Mean (SD)	**Extended-length** (N = 41) Mean (SD)	**P-value** *Unpaired t-student test*	**95% CI**
LDL-c	86.13 (28.61)	87.0 (24.71)	0.863	(-10.79, 9.05)
Systolic BP	129.07 (13.75)	127.48 (13.15)	0.508	(-3.14, 6.32)
BMI	29.54 (6.13)	28.87 (3.70)	0.506	(-1.32, 2.17)
HBA1C	6.84 (1.52)	6.45 (1.57)	0.351	(-0.43, 1.20)
	N (%)	**N (%)**	**P-value** *Chi-squared test*	**95% CI**
Tobacco	32 (18.6%)	5 (12.2%)	0.503	(-0.08, 0.18)
MACE	30 (17.4%)	5 (12.2%)	0.415	(-0.06, 0.17)

*Table 10 *BMI: body mass index; BP: blood pressure; CI: confidence interval; CR: cardiac rehabilitation; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; MACE: major adverse cardiac events; Pre: previous; Post: posterior; SD: standard deviation.*

8. DISCUSSION

Results of this long-term follow-up study show that the control of CVRF after discharge from the CR unit depends on which risk factor is analysed. The main result for LDL-c levels and tobacco consumption is that the improvement achieved with the CR has been maintained to year three, even though both have a trend towards deterioration along years. The observation for systolic BP, HbA1C in diabetic patients and BMI has shown a significant increase to year three and thereby, gains achieved for these risk factors are not maintained over the course of time.

The long-term control of CVRF after enrolment in a CR programme has been analysed in previous studies. In England, Willmer et al (57) analysed in a 5-year follow-up study, 143 patients, who had all completed standard CR programme, following ACS. Similar results to our study were found. They offered a supplementary programme in phase 4 of CR, including different types of healthy sport activities. Risk factor profile and other parameters were assessed. At 5 years of follow-up, the authors found a significant increase in the BMI and systolic BP, inferring deterioration in their control. For cholesterol and smoking they found no significance, and thus, a trend to maintenance up to year five. Results of the GOSPEL study, by Giannuzzi et al. (55) also showed similar findings. Authors demonstrated that up to 3 years, CR following ACS was effective in decreasing mortality, stroke, cardiac death and nonfatal AMI. However, they confirmed that improvements in the risk factors control and lifestyle behaviour achieved with the phase 3 programmes, were not maintained over the years. Other evidence, reported by a Canadian study (52), has found adherence rates and improved outcomes, not only at the end of the programme but also maintained over one year, in women. Furthermore, a Swiss study showed long-term maintenance in physical activity patterns and exercise tolerance after 2 years following a cardiac event, improving the risk factor profile (54).

In our study, the maintained LDL-c levels might be explained by the high compliance to the intensive statin therapy after ACS (21), even though secondary prevention is still far short from optimal (16). Maintenance of the low proportion of smokers along years could be resultant to the behavioural support and to the awareness against tobacco consumption (51). As aforementioned, improvement falls away for systolic BP, HbA1C in diabetic patients and BMI. These results might be hypothetically attributable to the low adherence on healthy diets and/or difficulties to maintain the weight loss achievements. To note, BMI target level has not been achieved overall time periods. All suggests that there is need for a reinforced dietary counselling and it would be useful to

include refresher sessions to address individual needs and thus, avoid time-related deterioration. It remains a future challenge for secondary prevention management.

Overall, the study suggests that maintaining healthy behaviours after a specialized CR prevention programme is problematic. The tendency in the risk factor control is time-related worsening, being consistent with observations of the prior studies. Some risk factors tend to be more controlled such as LDL-c and tobacco consumption, while others increase significantly after a period of time. However, it must be remarked that even though data for some risk factors reaches significance, little differences have been observed in the results. Thus, it might not have big effects on the patient. Otherwise, risk factors should not be underestimated given that minor changes have the potential to modify the risk factor profile and thereby, induce a substantial reduction in cardiovascular risk. (23) Longer-term support for behaviour change might be needed and community maintenance programmes may be useful. The results provide new evidence about the role of CR programmes in maintaining the long-term control of CVRF in ischemic cardiac patients. Further studies with larger population and longer follow-up might be advantageous to confirm our findings.

Our 3-year follow-up study results have shown short-term benefits in the control of CVRF, showing statistically significant improvements across all measures post CR. This is in accordance to international guidelines and recent evidence about the effectiveness of CR programmes (14). It reinforces the idea of CR implemented locally, such as Santa Caterina Hospital CR unit, is adequate for delivering the expected improvements. Otherwise, the recommended targets for risk factors control have been achieved only for HbA1C levels and systolic BP. This reveals that a large majority of coronary patients fail to achieve the recommended goals by the guidelines.

Baseline characteristics tend to be homogeneous among the study population and define a relatively low-risk population post-ACS. Mean age (56 years) is in accordance to Hedbäck et al (58) (57 years), whereas compared to a French study (33) (62 years) our study population is younger. Also, a large predominance of males participates in the CR programme, mostly young adults (< 65 years). This can be explained because prevalence of ACS is higher in men and also due to participation barriers in specific subgroups (women, older adults and ethnic groups) (3,38,40). At baseline, the proportion of patients with risk factors is high and thereby, defines a population which is mostly active-smoker, hypertensive, with hyperlipidaemia and overweight. It was the expected risk factor profile given that ACS is generally due to a combination of multiple CVRF.

Reported medications in our study are close to recommendations and thus, are in accordance to other secondary prevention studies. The EUROASPIRE IV study survey reported very similar data about cardioprotective treatment prescription (21). Noticeably in our study, most patients have been prescribed clopidogrel, which contrasts to the nowadays clinical practice where the new antiplatelet agents (prasugrel, ticagrelor) are more prescribed. It could be explained because subjects were enrolled in the study between 2008 and 2013, and new antiplatelet agents have been introduced during the last years.

The incidence of MACE in our study has been 16.4% and overall mortality 2.1%. Similarly, Giannuzzi et al, reported a 18.2% of MACE and 2.7% of mortality in a 3-year period of follow up (55). A Spanish study, by Maroto et al, reported a 7.7% mortality in a 10-year period of follow-up (51). According to these studies, the low rate of MACE reported could be attributable to the effectiveness of CR in reducing long-term mortality.

In regard to the duration of the CR programme, in our study no supplementary benefits of an extended-length programme have been found when compared to the standard-length CR programme. The aforementioned British study, by Willmer et al (57), identifies there are observable benefits in participating in long-term phase 4 CR programme. Authors in this study determined that those who declined the extended-length programme clearly did less well, since a significant increase in the parameters was reported. Hammill et al (59) determined that lower risk of mortality and morbidity is proportional to the number of rehabilitation sessions, as subjects attending all 36 sessions had lower risk compared to attending fewer sessions. In our study, several limitations regarding this secondary endpoint, as discussed in the following section, may explain our opposite results to the previous evidence.

8.1 Strengths and limitations

This study is characterized as representative of the CR secondary prevention strategy in Girona Area. We consider our data of interest because it is the first study to assess the benefits of the CR programme of Santa Caterina Hospital, and specially, the long-term benefits in which there is lack of evidence. It can be used as an initial study generating hypotheses for further studies. A high level of follow-up has been obtained as the proportion of patients lost to follow-up and/or who dropped out the study has been very low. Hence, the sample population analysed is near to the total CR population after ACS. Furthermore, homogeneity in data collection is ensured, as a single person has performed the collecting task. Finally, as a retrospective study, duration of the study has been short and without costs, so it has been highly feasible.

Several potential limitations warrant mention. Given that the study design is descriptive, no causality can be inferred and thereby, it does not allow affirming that variations observed are due to some cause. A multivariate analysis should complete the statistical analysis to assign associations and resolve which factors are responsible for the results seen. It is possible to have confounding variables, which we have not been able to adjust as no multivariate analysis has been done in our study.

In our study there was no control group. Ideally, it would have been advantageous to have a control group, being subjects after ACS without being referred to a CR unit, with similar baseline characteristics as the intervened group. This could have provided an important proof of the benefits of the CR programme in Girona health region. Furthermore, we consider that a different design using a long-term prospective follow-up study would have increased validity, because the variables would have been recruited during their appearance and could be validated and managed at the same time.

We analysed subjects that had already been referred for a CR programme, which justifies our low rate of excluded subjects. Referred patients are selected according to the inclusion criteria for CR (no comorbidities, no elderly, complications, ventricular arrhythmias, etc.). Thus, we had a pre-selected sample, being a relatively low-risk population. This reflects that we should have some caution in generalising our findings to the whole cardiac population, since this study refers to the patients enrolled in a CR programme following an ACS.

A selection bias was identified. The comparison between the two groups according the duration of the intervention may not be accurate. Groups were not blinded, but rather were driven by availability and patient's choice. The extended-length CR programme in Santa Caterina Hospital is not free of charge and this causes a barrier to access the intervention, since low-income population may not have the option. In the same line, other barriers for accessing CR exist as transport difficulties, work schedules, lack of perceived need, social commitments, etc. Moreover, people in the extended-length group may have a higher commitment to their personal health. Finally, the period of duration of the CR programme was heterogeneous and the proportion of patients was not the same in both groups. As a result, comparison does not truly represent the effects of prolonging the duration of the CR. More studies are required to clear up the true benefit on duration for improving the beneficial effects of CR programmes.

Retrospective review of clinical charts analyses pre-existing data, which is subject to an information bias. Some missing information was not available and could not be collected. Likewise, the tests and the established diagnoses of the included patients could not be controlled. Also, given that collected data was introduced in an electronic database, some data could have been not adequately collected. A second reviewer should have re-collected data to make the chart review more reliable.

Moreover, it is possible that the annual assessment visits provided to the patients allocated to usual care may have improved the prescription of medications and adoption of correct lifestyle habits, thus decreasing risk and possibly downplaying the benefit of the intervention. Furthermore, inter-observer variability may be considered. Systolic BP values already recorded were measured by different nurses at different times. Moreover, tobacco consumption might not be communicated to care providers due to a guiltiness feeling.

On the whole, this study involves one institution in the health region of Girona. Results could be extrapolated to very similar regions with a similar CR programme. Other studies would be necessary to predict the role of CR programmes in maintaining the CVRF control in different institutions and regions.

9. CONCLUSIONS

The control of LDL-c levels and tobacco consumption is maintained after a three-year period of follow-up among all patients referred to the hospital-based CR programme of Santa Caterina Hospital from Girona area, after suffering an ACS. However, a significant increase of systolic BP, BMI and HbA1C levels has been found at long-term.

Short-term benefits regarding CVRF control have been observed in the CR unit of Santa Caterina Hospital. However, the recommended targets for risk factors control have been achieved only in HbA1C levels and systolic BP.

The majority of the population analysed are young male adults, diagnosed of STEMI, with preserved ejection fraction. The baseline risk factor profile defined a population which was active-smoker, hypertensive, with hyperlipidaemia and overweight.

The incidence of MACE among all patients post-ACS has been 16.4%.

No significant differences in the benefits achieved have been found between a standard-length and an extended-length CR programme among all patients enrolled in the CR programme of the Santa Caterina Hospital in Girona, after suffering an ACS.

10. ETHICAL CONSIDERATIONS

The project has been conducted in accordance to the ethical principles established by the World Medical Association in the *Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects*, and it has respected the Good Clinical Practice guidelines. Likewise, this study has been approved by CEIC of the Hospital Universitari Dr. Josep Trueta of Girona (see Appendix C).

The researchers were committed to ensure compliance with the principles set out in the "*Ley Orgánica 15/1999 de Protección de Datos de Carácter Personal"* of 13th of December, and its development in the Royal Decree 994/1999 of Security measures for automated files containing personal data, and in the Royal Decree 1720/2007 of the Development of the organic law on data protection. According these existing national laws, the treatment, communication and transfer of personal data of all patients was protected, guaranteeing the privacy of all the participants, freedom and fundamental rights of physical people, as well as the confidentiality of their personal information. In order to guarantee confidentiality of the study data, content of the database was encrypted and protected from uses not allowed by persons outside the investigation and therefore it was considered strictly confidential. Patient identities will remain confidential according to the aforementioned law in any presentation of the results of this study at meetings or in publications.

The study has been carried out in accordance with the requirements set out in the international standards for epidemiological studies, as recorded in the International Guidelines for Ethical Review of Epidemiological Studies (Geneva, 1991). It defines the principles that must be scrupulously respected by all persons involved in the investigation, as well as the legislation in force in Spain in accordance with Ministerial Order SAS / 3470/2009, regarding the conduct of observational studies.

All patients gave written informed consent to participate in the pilot programme of CR authorizing maintenance of a secure computerized database with their personal data available for future research studies (see Appendix D). Since it is a retrospective observational study and CR patients signed the informed consent for the CR programme, the lack of an explicit informed consent for the study is justified and given the approval by CEIC. Moreover, this is a study without risk seen that there will be no changes on the biological, psychological, physiological or social conditions of the patients.

11. WORK PLAN

Phase 1: Project design (February – December 2016)

The first meeting of the research team was in the 9th of February 2016. The main topic of the research study was decided and the execution plan was established. A comprehensive and exhaustive bibliographic research was done during the following months in order to elaborate the protocol, which was later presented and approved by the CEIC (see Appendix C). After establishing the methodology of the project, the database was created with the main variables that had been ulterior collected by the main researcher.

Phase 2: Data collection (December 2016 - January 2017)

Data of the patients included in our study was retrospectively registered in an electronic database by assessment of the computerized clinical charts. All data was encrypted to guarantee the confidentiality of patient's data. A final review of the database was done before conclusion in order to avoid possible errors.

Phase 3: Statistical analysis (January 2017)

Once the data base was concluded, the main researcher did a descriptive analysis of the data. A bivariate analysis with the appropriate statistical tests was done by the main researcher and a qualified statistician.

Phase 4: Interpretation of the results and conclusions (January 2017)

The outcomes of the study were interpreted and discussion of the results was done along with the final conclusions.

Phase 5: Final report elaboration (January 2017)

A report with the final results, discussion and conclusions was elaborated. Limitations of the study were considered.

Phase 6: Scientific publications and dissemination of data (February – May 2017)

Dissemination strategy consists on performing local meetings and conferences in Girona during the following months. This study aims to be published in the journal of Spanish Society of Cardiology. The cardiology team will participate in the national congress of the Spanish Society of Cardiology (SEC) and in the ESC congress in order to diffuse the results and conclusions of the study.

12. STUDY CHRONOGRAM

PHASES	2016											2017					PERSONAL
	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	
PHASE 1: PROJECT DESIGN																	
Topic decision and execution plan																	Cardiology team
Bibliography research																	Research team
Protocol elaboration																	
Creation of the database																	
Evaluation and approval of the study protocol by CEIC*																	CEIC
PHASE 2: DATA COLLECTION																	
Selection of patients suitable for the study																	Main researcher
Clinical charts revision and fulfilment of the electronic database																	
Final review of the database																	
PHASE 3: STATISTICAL ANALYSIS																	
Descriptive analysis																	Main researcher
Bivariate analysis																	Main researcher and statistician
PHASE 4: RESULTS INTERPRETATION AND CONCLUSIONS																	Main researcher
PHASE 5: FINAL REPORT ELABORATION																	
PHASE 6: SCIENTIFIC PUBLICATIONS AND DISSEMINATION OF DATA																	Cardiology team

Table 11 – Study chronogram

**CEIC: Clinical and Ethical Investigation Committee*

13. BUDGET

All tasks of the study related with the protocol design, bibliography research, data collection, interpretation of results and final report elaboration have been performed by the research team. The team has also been able to do the statistical analysis with the guidance of a qualified statistician. It has not been necessary for any worker to receive any financial compensation.

Regarding the goods and services, a computer laptop with SAP access was available at the hospital. The costs attributable to its use are included in the routine clinical practice expenses.

Diffusion of the final article is task of the research team, but a translation service will be necessary in order to publish the definitive article. This study is expected to be published in the journal of Spanish Society of Cardiology (SEC). Likewise, the researchers will participate in the national congress of the SEC and in the ESC congress in order to diffuse the results and conclusions of the study. All costs of the study are shown in Table 12.

BUDGET	COST	QUANTITY	SUBTOTAL
Personnel expenses			
▪ The researchers do not receive any financial compensation for their contribution to the study	0 €/hour	0	0 €
Goods and services procurement			
▪ Computer……..	free	1	0€
▪ Translation service……..	40€/hour	10 hours	400€
Publications fee			
▪ Publication in the journal of SEC	free	1 unit	0€
Dissemination, travel and subsistence costs			
▪ Local meetings and conferences in Girona area	80€	4 meetings	320€
▪ National congress of the SEC 2017 attendance			
o Inscription……	400€		800€
o Travel ……..	150€	2 people	300€
o Accommodation ……	300€		600€
▪ International ESC Congress 2017 attendance			
o Inscription……	850€		1700€
o Travel ……..	150€	2 people	300€
o Accommodation ……	350€		700€
TOTAL:			**5.120€**

Table 12 – Study budget.

**SEC: Sociedad Española de Cardiología; ESC: European Society of Cardiology.*

14. CONFLICTS OF INTEREST

All members of the study declare no conflicts of interest.

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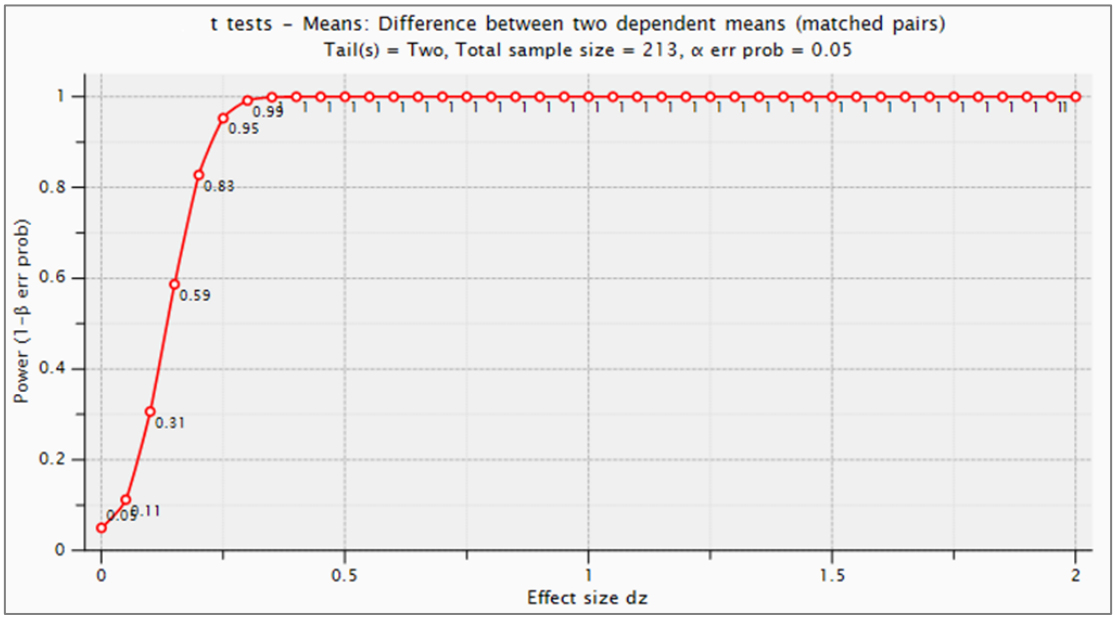
16.1 **Appendix A.** Sample statistical power (Gpower Version 3.1.9.2.)



16.2 **Appendix B.** Data collection form (fulfilled by the main researcher)

COLLECTED DATA	BASAL	PRE CR programme	POST CR programme	YEAR 3
Participant number	X			
Gender	X			
Age (years)	X			
Weight (kg)	X			
Height (metres)	X			
Type of ACS	X			
EF (%)	X			
Tobacco consumption	X			
Hypertension	X			
Diabetes mellitus type 2	X			
Hyperlipidaemia	X			
Depression	X			
P2Y12 therapy	X			
β -blockers	X			
ACEI /ARBs	X			
Statins	X			
Systolic BP (mmHg)		X	X	X
BMI (kg/m^2)		X	X	X
LDL-c (mg/dL)		X	X	X
HbA1C (%)		X	X	X
Tobacco consumption		X	X	X
MACE				X

**ACEI: angiotensin-converting-enzyme inhibitor; ACS: acute coronary syndrome; ARBs: angiotensin II receptor blockers; BMI: body mass index; BP: blood pressure; CR: cardiac rehabilitation; EF: ejection fraction; HbA1C: glycosylated haemoglobin; LDL-c: low-density lipoprotein cholesterol; MACE: major adverse cardiac events.*

16.3 **Appendix C**. CEIC approval letter

Hospital Universitari de Girona
Doctor Josep Trueta

Avinguda de França s/n.
17007 Girona
Teléfon 972 940 200
www.gencat.net/ics/trueta

Marta Riera Juncà, Secretària del Comitè d'Ètica d'Investigació CEI GIRONA, amb domicili a l'Hospital Universitari de Girona Dr. Josep Trueta Avinguda de França s/n 17007 Girona

CERTIFICA

Que el Comitè d'Ètica d'Investigació CEI GIRONA, segons consta en l'acta de la reunió celebrada el dia 20/12/2016 ha avaluat el projecte: **Beneficios del programa de rehabilitación cardíaca a largo plazo: 3 años de seguimiento. Cod Beneficios. V.** en català i castellà, amb la Sra. ELENA CANAL GARCÍA com a investigadora principal.

Que els documents s'ajusten a les normes ètiques essencials i per tant, ha decidit la seva aprovació.

I, perquè consti, expedeixo aquest certificat.

Girona, a 11/01/2017

Hospital Universitari de Girona
Doctor Josep Trueta
Comitè Ètic
d'Investigació Clínica
Institut Català de la Salut

Generalitat de Catalunya
Departament de Salut

Institut Català de la Salut

16.4 **Appendix D.** Information document and informed consent for participating in the CR programme of Santa Caterina Hospital

Hospital Universitari de Girona Doctor Josep Trueta — Institut d'Assistència Sanitària — Hospital Santa Caterina

HOJA DE INFORMACIÓN. CONSENTIMIENTO INFORMADO

¿Qué es la Rehabilitación Cardíaca?

La Rehabilitación cardíaca es el conjunto de intervenciones múltiples y coordinadas diseñadas con el fin de optimizar las condiciones físicas, psicológicas y sociales, además de estabilizar, retrasar e incluso revertir la progresión de la enfermedad cardíaca; con la consecuente disminución de la morbimortalidad.

La creación de unidades de Rehabilitación cardiaca fue propuesta por la Organización Mundial de la Salud (OMS) en los años 60 'y desde entonces se han ido implantando a un gran número de países. A pesar de haberse confirmado, mediante estudios científicos, los grandes beneficios en cuanto a la salud física, psicológica, calidad de vida, etc. en nuestro país son escasos los centros que disponen de estos programas.

Los programas de Rehabilitación Cardiaca están dirigidos a pacientes con problemas cardíacos (pacientes con infarto de miocardio y / o angina, cirugía de bypass, insuficiencia cardíaca, portadores de stents...) e incluyen sesiones de entrenamiento físico, de pautas de actuación psicológica (control del estrés, técnicas de relajación, actitud vital...) y de control de los llamados factores de riesgo cardiovascular (tabaco, hipertensión arterial, colesterol elevado, obesidad, etc).

Fases de la Rehabilitación Cardiaca

Básicamente consta de 4 fases:

1. Fase I (intrahospitalaria): mientras esté ingresado en el hospital, recibirá las primeras "charlas educativas" por parte del personal de enfermería respecto a su enfermedad, factores de riesgo, hábitos alimenticios... Así como se le indicarán las pautas a seguir una vez sea dado de alta y comience la fase III.

2. Fase II (ambulatoria): Desde la alta hasta después de unas 2-3 semanas (que será citado por el cardiólogo), iniciará las pautas de ejercicio físico, dieta, etc. Que se le habrán explicado en la fase I. Durante este tiempo, será citado por el psicólogo de la Escuela de Rehabilitación Garbí, donde se hará una valoración de la adecuación a estas pautas, podrá solucionar dudas, etc.

3. Fase III: Al cabo de 2-3 semanas del alta hospitalaria y, después de la visita con el psicólogo, será citado en el Parque Hospitalario Martí Julià de Salt (Girona) para tener la primera visita con el cardiólogo y realizar una prueba de esfuerzo. Se recomienda llevar el

informe de alta médica y asistir con ropa y calzado cómodo. La prueba de esfuerzo consiste en caminar sobre un tapiz rodante, que cada 3 minutos va aumentando de velocidad y pendiente. Según el resultado de esta prueba y la valoración cardiológica, se le puede ofrecer continuar en el Programa de Rehabilitación Cardiaca. Si es así y acepta, en el periodo de 1-2 semanas será citado a ir a "la Escuela de Rehabilitación Garbí", para iniciar el siguiente programa: Sesiones periódicas (3 veces a la semana durante 12 semanas) de ejercicio físico, visitas con el psicólogo y nutricionista que serán impartidas y supervisadas por el equipo de Rehabilitación Cardíaca (cardiólogo, médico rehabilitador, fisioterapeuta, psicólogo, nutricionista). Al finalizar la 12ª semana, se le volverá a repetir la prueba de esfuerzo y la visita con el cardiólogo para valorar los resultados.

Durante los 3 meses siguientes se realizarán sesiones similares pero únicamente 1 vez al mes. Una vez completada esta fase, se realizará una nueva prueba de esfuerzo y una visita final con el cardiólogo, quien le dará un informe de alta con todos sus resultados.

4. Fase IV (de mantenimiento): durante el resto de la vida. Consiste en mantener los hábitos de vida aprendidos durante las fases previas. Seguimiento por parte del médico de cabecera y cardiólogo de zona (no contemplada en el Plan Piloto).

Aunque son muy excepcionales y raramente graves, puede darse el caso de alguna complicación durante todo el proceso (lesiones musculares, angina, arrítmias...). No obstante, los centros donde se realizan estas actividades se encuentran perfectamente equipados, tanto desde el punto de vista técnico como de personal, para actuar y solucionar cualquier complicación que se presente.

CONSENTIMIENTO INFORMADO

Yo_____, con DNI _____, después de haber leído el texto anterior y aceptando las condiciones, actividades y riesgos que supone, acepto ser incluido y formar parte del Plan Piloto de Rehabilitación Cardiaca. Del mismo modo, acepto que mis datos (siempre y cuando se mantenga la confidencialidad correspondiente) sean utilizados con finalidad científica y / o mejora del sistema sanitario. Confirmando que mi participación es voluntaria y que en cualquier momento del proceso puedo abandonar el programa:

Firma del paciente

DNI

A___de_____del 2008

Firma del médico

DNI

A___De_____del 2008