Journal of
Cardio - Thoracic Medicine

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Cardiac Rehabilitation and Secondary Prevention Program effect in Chronic Total Occlusion Percutaneous Coronary Intervention patients

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ARTICLEINFO

Article type:
Original Articles

Article history:
Received: 20 April 2021
Revised: 26 May 2021
Accepted:17 July 2021

Keywords:
Chronic Total Occlusion
Secondary Prevention
Percutaneous Coronary Interventionism

ABSTRACT

Introduction: Chronic Total Coronary Occlusion has a high risk of mortality associated with Acute Coronary Syndrome with significantly ventricular disfunction reflected in functional class patient by intolerance to perform physical effort. The Percutaneous Coronary Intervention is the gold standard approach, but in many patients this procedure is not successful. Cardiac Rehabilitation and Secondary Prevention Programs has showed improve the patient's ability to perform physical effort by its positive effect on endothelial function and promote angiogenesis, increasing the ischemic threshold. We evaluate the Cardiac Rehabilitation and Secondary Prevention program effect on myocardial performance and ischemic profile in successful and unsuccessful Chronic Total Occlusion Percutaneous Coronary Intervention patients.

Materials and Methods. A non-randomized clinical trial was conducted in patients with CTCO underwent to Percutaneous Coronary Intervention (PCI). Patients were divided into two groups: 1) With successful PCI and 2) With unsuccessful PCI. All patients underwent a Sestamibi-Dipyridamole cardiac scan and stress test before and after of CRH&SP. The cardiac rehabilitation program considered 4-6 weeks of 5 weekly 30-minute training sessions with aerobic at 70% of Heart Resistance Reserve (HRR), with interspersed 3 weekly strength training sessions, as well as nutritional and Psychiatric group interventions.

Results. We evaluated 25 patients with successful PCI (n = 13) and unsuccessful PCI (n = 12). For both groups, the CRH&SP showed significant improvement ($p < 0.05$) in myocardial performance parameters, ischemic profile, and physical effort tolerance, with a Cohen's Delta ≥ 80% in Nuclear Medicine Risk, NYHA functional class, METs reached, oxygen consumption, Myocardial Efficacy Index and Duke Score.

Conclusions. The CRH&SP has a high positive effect on ventricular function improvement, myocardial performance, and ischemic profile in patients with Chronic Total Coronary Occlusion.

►*Jorge Antonio, L., Hernández-Esparza, T., Puente-Barragán, A., Morales- Portano, J., Gómez-Álvarez, E., Merino-Rajmé, J., Leyva-Valadez, E., Aceves-Chimal, J. Cardiac Rehabilitation and Secondary Prevention Program effect in Chronic Total Occlusion Percutaneous Coronary Intervention patients.J Cardiothorac Med. 2021; 9(3):* 839-844

Introduction

Chronic Total Coronary Occlusion (CTCO) have significant harmful ischemic effects on ventricular function that limit the patient's functional class despite the underlying collateral circulation sometime shown by

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Sestamibi-Dipyridamole myocardial perfusion scan (1-5). In patients with chronic ischemia, successful coronary intervention has shown improvement in quality and life expectancy even in multivascular disease treated with hybrid procedure (Surgical and endovascular revascularization) (6). However, the "ISCHEMIA Clinical Trial" study in 3.2 years follow-up of patients with clinically stable moderate to severe ischemia did not observed differences in reduction of mortality risk of mortality or cardiovascular new events (7).

The Cardiac Rehabilitation and Secondary Prevention Programs (PRHC&PS) consider interdisciplinary therapies based on physical training, cardiovascular risk factors control, nutritional and psycho-emotional support, had shown improvement in physic effort tolerance probably by improve endothelial function and promote angiogenesis in ischemic patients as is mentioned in several studies, showing a mortality rate decreasing when the volume training is finished in its entirety (8-14).This CRH&SP beneficial effect on endothelial function could due to the inflammatory regulation by biochemical anti-inflammatory, anti-proliferative, anti-adhesive platelet, fibrinolytic and vasodilator mediators, which are stimulated by a supervised physical training that modulates the atheromatous plaque and myocardial oxygen consumption improvement (15-20).

Has been logically considered that the percutaneous interventionism in patients with CTCO is responsible for the clinical improvement of the patient; however, it has been hypothesized that CRH&SP could have a similar effect on physical effort tolerance and finally on clinical improvement inclusive in patients with unsuccessful Percutaneous Coronary Interventionism procedure. We evaluated the results of a non-randomized clinical trial to discern this hypothesis.

Materials and Method

The study was made in a Tertiary Medical Care Center "CMN 20 de Noviembre ISSSTE", located in Mexico City, Mexico and was approved by hospital research and ethic committees. Patients undergoing to Percutaneous Coronary Intervention by chronic total occlusion in NYHA functional class II were eligible and signed an informed consent. Patients were assigned to each group in accord with PCI procedure results: Group 1) With successful results and 2) With unsuccessful results with only diagnostic angiography and were not eligible to Coronary Artery Bypass Graft (CABG).

Patients in both groups were stratified according to their tolerance to physical exertion from Duke score and cardiovascular risk with ATP III Score. Patients with physical effort tolerance > 60% on theorical oxygen consumption (VO2p) without ischemic threshold initial stress test were assigned to 4 weeks of training and with VO2p < 60% and/or with ischemic threshold to 6 weeks of training.

Physical training method:

The rehabilitating cardiologist supervised all sessions training by continuous electrocardiographic monitoring and made the prescription of training modality about frequency, intensity, duration, volume, and type of exercise in 2 alternated modalities of physical exercise:

1. Five times a week, 30 minutes daily of aerobic exercise at 70% of the Heart Rate Reserve (HRR) calculated with Karvonen formula.
2. Three times a week, exercise of strength and bio motor skills at 40% of previous load that patient was lift capable before start exercise (1RM).

Simultaneously, by an interdisciplinary team were carried out complementary educational interventions in personalized and group sessions: A personalized dietary by a nutritionist, teach how control risk factors by a cardiologist; exercise technics by a cardiovascular physiotherapist and anti-stress techniques, emotional control, anti-smoking techniques, occupational therapy, and sexuality by a psychiatrist.

Before and after CRH&SP, ventricular performance and ischemic profile were evaluated with follow studies:

Sestamibi-dipyridamole Cardiac Gamagram: LVEF at rest and stress, LVEF drop change, Left Ventricle End-systolic Volume (LVSV) and End-diastolic Volume (LVDV).

Exercise Test: METs achieved at maximum effort, Peak oxygen consumption (VO2p), Myocardial Efficiency Index (MEI), VO2p/DP ratio, Heart Rate Reserve (HRR), Double Product (DP) as a surrogate of

myocardial oxygen consumption, Duke Score, and ischemic threshold in accord with angina symptoms and/ or electrocardiographic changes characterized by ST segment elevation or depression in two or more contiguous leads.

Statistical analysis

The variables description was performed with mean and standard deviation. The variables comparison was done with student's t and Chi2 test.

The PRHC&PS size effect was determined with Cohen Delta test. A p value < 0.05 was considered as statistical significance.

The analyzis was made with SPSS package v26.0 for Windows Operative System (Chicago, Il, USA).

Results

We included 25 patients with high cardiovascular risk (ATP-III > 20 points), in group with successful PCI (n = 13) and unsuccessful PCI (n = 12) by SYNTAX score > 33 points.

No significant differences were observed between groups in demographic variables, cardiovascular risk factors, severity of myocardial ischemia, damaged coronary arteries, infarcted myocardial tissue, and blood chemistry parameters (Table 1).

In both groups, before and after CRH&SP, was observed a significant improvement (p <0.05) in myocardial performance parameters (VO2, MEI and functional class), in ischemic profile (Nuclear Medicine Risk, Duke Score and LVSV) and physical effort tolerance (METs and Myocardial Efficiency Index), but did not showed differences in LVEF at rest, stress, delta change, LVDV and ischemic threshold with size effect > 80% in Nuclear Medicine Risk, NYHA functional class, METs achieved, myocardial oxygen.

Table 1: Cardiovascular Risk factors, coronary affected and myocardial perfusion findings in patients with Chronic Total Coronary Occlusion undergoing to Percutaneous Coronary Intervention

	Percutáneous Coronary Intervention		
	Successful (n = 13)	**Unsuccessful (n = 12)**	**p**
Sex			
Male (n)	5 (38%)	6 (50%)	0.43
Female (n)	8 (62%)	6 (50%)	
RISK FACTORS			
Hypertension (n)	12 (92%)	11(91%)	0.74
Diabetes Mellitus (n)	7 (53%)	7(58%)	0.97
Dyslipidemia (n)	11 ((84%)	11(91%)	0.97
Smoking (n)	9 (69%)	9 (75%)	0.97
Chronic Kidney Disease (n)	3 (23%)	2 (16%)	0.54
CORONARY AFFECTED			
Main Left Coronary (n)	1 (7%)	2 (8%)	0.18
Anterior Descending (n)	9 (69%)	11 (91%)	0.38
Circunflex Coronary (n)	8 (61%)	9 (75%)	0.36
Right Coronary (n)	9 (69%)	10 (83%)	0.58
MYOCARDIAL ISCHEMIA			
Sever (n)	7 (53%)		
Moderate (n)	10 (76%)	6 (50%)	0.94
Mild (n)	10 (76%)	10 (83%)	0.53
MIOCARDICAL INFARCTION		9 (75%)	0.63
Transmural (n)	6 (46%)		
No Transmural (n)	11 (84%)	4 (33%)	0.40
		12 (100%)	0.26

P-Value was calculated with chi-squared test

Table 2: Cardiac Rehabilitation and Secondary Prevention Program (CRS&SPP) effect in patients with Percutaneous Coronary Intervention successful and unsuccessful

	Interventional Coronary Percutaneous						
	Successful			Unsuccessful			
	Pre	Post	p	Pre	Post	p	Size effect
LVEF rest %	52±13	54±12	0.81	40±3	50±2	0.11	92
LVEF stress %	43±12	44±11	0.80	45±5	52±3	0.12	80
LVEF Delta-Change	9±1	10±2	0.79	5±2	2±1	0.14	60
Left Ventricle Systolic Volume [ml]	96±17	85±16	0.41	121±12	114±17	0.46	78
Left Ventricle Diastolic Volume [ml]	113±15	110±14	0.39	112±28	101±15	0.39	56
Nuclear Medicine Risk	2.5±0.3	1.6±0.2	0.01	2.5±0.5	1.5±0.2	0.02	86
NYHA Functional Class	1.8±0.3	1.3±0.4	0.01	2.1±0.3	1.1±0.9	0.01	80
METS [VO2/kg/min]	5.6±2	8.2±1.8	0.02	5.1±2	7.5±2	0.02	91
Oxygen Consumption [ml/kg/min]	19.9±7	28.3±7	0.01	20±5	25±6	0.03	84
MEI [Watts/kg x 10^{-2}/ASC]	10.3±3	7.2±3	0.01	9.3±3	6±1.6	0.01	85
Ischemic Threshold [bpm]	79±15	69±12	0.32	72±18	50±12	0.02	54
Duke Score	5.2±2	6.4±2	0.89	5.2±3	6.5±2	0.42	80

LVEF: Left Ventricular Ejection Fraction; NYHA: New York Heart Association: METS: Metabolic Unit; MEI: Myocardial Efficacy Index; PCI: Percutaneous Coronary Intervention; p value was calculated with t Student test and Size Effect with the Cohen Delta test.

Discussion

Cardiac Rehabilitation program's main purpose is essentially focused on improving the patient's quality of life and allowing integration to their work activity. The innovation in the current Rehabilitation Programs (CRH&SP) consist in a supervised physical training, supported by nutritional and psychological assistance for the control of cardiovascular risk factors, psycho-emotional attention with occupational therapy and anti-smoking techniques with apparently better sexual efficacy, maybe as a improve in oxygen consumption (VO2) in striated muscle and in metabolic profile through anti-inflammatory mediators stimulated by physical training that promotes a scenario that would allow endothelial repair and angiogenesis (19-22).

Patients with chronic coronary damage and anatomical characteristics that prevent open the affected coronary arteries usually have poor quality life and lower survival. These patients, with unsuccessful coronary intervention, are a challenge to integrate them a physical training program because have high risk of myocardial infarction and even sudden death (4-7). Nevertheless current Cardiac Rehabilitation Programs

Consider a supervised physical training supported with a nutritional and psychological team that could allow include them.

In this study, we observed a positive impact of CRH&SP on myocardial performance parameters and physical effort tolerance with similar results in patients with successful and unsuccessful PCI (Size effect > 80%), especially in variables with prognostic value of survival, so we could be assumed that CRH&SP was responsible to improvement seen and thus, it should be implemented. Also, in patients with multivessel coronary illness with ICP unsuccessful.

The ISCHEMIA clinical trial (7), showed in patients with moderate to severe ischemia that interventional treatment has not advantages over conservative treatment to long time on cardiovascular risk reduction which supports our considerations on CRH&SP and represents a very good alternative treatment to patients with unsuccessful PCI, because with an appropriate dose and volume of training is possible produces a cascade of pan-vascular benefits capable of improving not only the ischemic profile of patients with COTC and severe ischemia but also in myocardial

performance expressed in METs, Oxygen Consumption and functional class (23, 24).

It was logic expect null or low improvement in PCI unsuccessful patients group after the CRH&SP, assuming that the opening of the coronary arteries in PCI successful patients, would provide greater blood flow to myocardial tissue and therefore would significantly improve the contractile function of cardiac muscle by disappear of myocardial ischemia, however, this hypothesis was rejected by our findings that shown an positive impact of Cardiac Rehabilitation Program in both groups, although with high size effect of PCI (Table 2).

In myocardial perfusion scenario evaluated with myocardial scintigraphy, we also observed significant differences ($p < 0.05$) after application of CRH&SP with a positive effect and with significant reduction in Nuclear Medicine Risk ($p = 0.001$), which supports the possibility of angiogenic stimulation as adaptation to physical training, improving myocardial perfusion possibly by development of collateral circulation. This is supported by Martínez[12] and Giallauria(14) who describe that early physical training after a myocardial infarction reduces microvascular dysfunction, hypoperfusion and improves ventricular function.

There is no doubt about physical training has a positive effect at peripheral and central level, improving endothelial function and increasing size and number of mitochondria in cardiac and striatum muscle, which is reflected in oxidative capacity and oxygen consumption, avoiding that patient release catecholamines in rest and physical stress, decreasing the renin-angiotensin-aldosterone activity and in consequence of peripheral vascular resistance, in addition to impact on respiratory system, increasing vital capacity, oxygen diffusion and ventilatory kinetics through conditioning of respiratory and accessory muscles (9, 10). Furthermore before mentioned, we consider that nutritional and psychological counseling for control of cardio-metabolic risk factors and decrease in psychological stress essentially represented by events of depression and anxiety allowed achieve comprehensive results which is essential in the care of patients with any cardiopathy.

In sum, despite the small sample size evaluated in this study, the evidence shows a high beneficial effect of CRH&SP on ventricular performance and myocardial perfusion in patients with Chronic Total Coronary Occlusions independently of PCI results, so physical training intervention with nutritional and psychological counseling could be a strong alternative treatment to patients with CTCO not candidates to endovascular or surgical revascularization.

Conclusion

Cardiac Rehabilitation and Secondary Prevention Program has a positive effect on ventricular function improvement, myocardial performance, and ischemic profile in patients Chronic Total Coronary Occlusion regardless of Percutaneous Coronary Intervention result.

The CRH&SP positive effect on ventricular function improvement, myocardial performance, and ischemic profile in patients with Chronic Total Coronary Occlusion has an adjuvant effect together with Percutaneous Coronary Interventionism.

Interest Conflict

Do not exist any conflict to declare

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