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Impact of Chronotropic Incompetence and Correlation with Exercise Tolerance in Patients with Implantable Cardiac Devices Undergoing a Phase II Cardiac Rehabilitation Program

José L. Martinez-Paniagua[1,2*], Jorge A. Lara-Vargas[1,2], Erik E. Briceño-Gómez[1,2], Hugo A. Radillo-Alba[1,2]
[1]Cardiac Rehabilitation Service, Modular Services Division, 20 de Noviembre National Medical Center, Mexican Social Security Institute
[2]School of Medicine, La Salle University; Mexico City, Mexico

ABSTRACT

Objective: Since patients with implantable cardiac devices tend to develop chronotropic incompetence (CI) associated with the effect of the device itself or the pharmacological effect of the underlying disease, CI could act as a limiting factor in improving exercise tolerance in patients undergoing cardiac rehabilitation program, since an increase in HR is a crucial part in improving cardiac output as a central component of oxygen consumption (VO2). However, it has been observed that there could be other factors contributing to the improvement in exercise tolerance in these patients regardless of the presence of CI. The aim of this research is to clarify the effect of chronotropic incompetence on the improvement in exercise capacity in patients with implantable cardiac devices after a phase II cardiac rehabilitation program (CRP).
Methods: Quasi-experimental study applied to patients with implantable cardiac devices (ICDs, CRT, pacemakers) undergoing a supervised concurrent CRP, lasting 4-6 weeks, at an intensity between 65-80% of heart rate reserve (HRR), associated with kinesiotherapy sessions (with strength and endurance training and other biomotor qualities) and interdisciplinary intervention, education, and counseling. CI was calculated using the chronotropic response index, and METs-load measurement was performed at the beginning and at the end of the intervention.
Results: Forty patients with a mean age of 61.4 years were included, mostly male (29) 72.5%, (23) 57.5% diagnosed with heart failure, and regarding the type of device, pacemakers (20) 50%, implantable cardioverter-defibrillator (ICD) (12) 30%, and cardiac resynchronization therapy with defibrillator (CRT-D) (20) 8%, of the total patients (35) 87.5% presented chronotropic incompetence and only (5) 12.5% with normal chronotropic response at the end of the intervention. A significant decrease in the chronotropic response index from 0.70 to 0.47 ($p < 0.001$) and a significant increase in METs-load from 5.47 to 9.35 ($p < 0.001$) were found. The value of the differential between initial and final METs (delta-METs) was obtained for both groups, observing a significant increase between initial and final METs in favor of patients with CI (3.8 Vs 3.5, $p < 0.012$) at the end of the intervention. A significant moderate negative correlation ($r = -0.395$, Spearman, $p < 0.012$) was determined between the degree of CI and final METs-load.
Conclusions: It was observed that patients with implantable cardiac devices undergoing a CRP show an increase in exercise tolerance measured in METs, with an inversely proportional correlation to chronotropic incompetence.

KEYWORDS: chronotropic incompetence. Chronotropic response index. Exercise tolerance. Cardiac rehabilitation program

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INTRODUCTION

The increasing use of implantable cardiac devices, such as pacemakers, implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT), poses challenges and opportunities in the field of cardiac rehabilitation. Despite the potential benefits of these devices on cardiac function and survival, many patients with these devices may have reduced exercise tolerance due to fatigue, dyspnea, and chronotropic incompetence (CI) [1,2,3,4]. CI, characterized by an inadequate increase in heart rate during exercise, has been considered a significant contributor to exercise intolerance in this population [7]. Chronic heart failure with severe left ventricular dysfunction is a condition that often requires the use of implantable cardiac devices and is associated with reduced exercise tolerance [5,6,7]. Despite the demonstrated mortality benefits of a reduced resting heart rate, many patients do not achieve optimal doses of heart rate-reducing agents, possibly due to fear of inducing further exercise intolerance and worsening symptoms [8]. However, the majority of patients with implanted electronic devices can benefit from phase II cardiac rehabilitation (CR) programs [2].

Understanding the technology of pacemakers and implantable cardioverter-defibrillators (ICDs), as well as cardiac resynchronization therapy (CRT), is important in exercise prescription [1]. Cardiac implantable electronic devices are usually programmed at rest, but their evaluation during exercise can provide important clinical information, especially in patients with chronotropic incompetence or devices programmed for rate response [13]. Physical training is a key component of a CR program, which, along with device functions, can have a significant synergistic effect on cardiac function [3]. CR programs are essential for optimizing medical treatment, improving exercise capacity, and monitoring the proper functioning of devices. It has been shown that physical training, whether aerobic or resistance, produces beneficial adaptations in cardiovascular and muscular function, including increased systolic volume, improved contractility, and reduced resting heart rate [12,13,14,15].

Dynamic or aerobic endurance exercise has been demonstrated in multiple studies to impose the greatest demand on the cardiopulmonary system, with a linear relationship between oxygen consumption (VO2) and exercise intensity. Cardiovascular and functional adaptations related to physical exercise, such as increased cardiac output, increased stroke volume, and reduced resting heart rate, translate into improved exercise tolerance and VO2 [6]. On the other hand, strength training produces a moderate increase in cardiac output with little increase in oxygen consumption and a modest but significant increase in left ventricular wall thickness without affecting systolic or diastolic function [9]. Additionally, this type of training can increase the arteriovenous oxygen difference, leading to better oxygen extraction by active muscles [10]. With increased strength, muscle mass, and aerobic endurance, not only does the heart's ability to pump blood more efficiently improve, but also the need for a lower heart rate to sustain the same stroke volume at rest [16,17,18].

It is widely recognized in multiple reviews that VO2 has been shown to be a predictor of mortality, and that concurrent training increases maximum exercise capacity by increasing stroke volume and arteriovenous oxygen difference, with a decrease in resting heart rate due to its positive effects on the autonomic nervous system, with a decrease in sympathetic hyperactivity and an increase in R-R interval variability [11,12,13]. Thus, CR programs that include physical exercise, both aerobic and resistance, as well as respiratory muscle training, can play an important role in improving exercise capacity, quality of life, and survival in patients with implantable cardiac devices. [18,21] These programs should be individually tailored to address the specific needs and limitations of each patient, and in those with devices, the "physiological brake" of training on heart rate (CI) could reduce physical performance (VO2) [22,23].

We are interested in the relationship between CI and exercise tolerance measured in METs in patients with implantable cardiac devices undergoing a CR program. We hypothesize that the presence of CI will correlate with a decrease in the improvement in exercise tolerance in patients with implantable cardiac devices undergoing a concurrent CR program. The main objective of our study is to determine if the presence of CI is correlated with a decrease in the improvement in exercise tolerance measured in METs in patients with implantable cardiac devices undergoing a concurrent CR program.

METHODS

A quasi-experimental study was designed, applied to a cohort of 40 patients, with implantable cardiac devices (ICDs, CRT, pacemakers), who underwent a phase II cardiac rehabilitation (CR) program and interdisciplinary intervention, at the Cardiac Rehabilitation Service of the National Medical Center 20 de Noviembre, during the period from April 1, 2018, to December 31, 2023. Patients over 18 years of age, of both sexes, with any diagnosis, and carrying implantable cardiac devices (ICDs, CRT, pacemakers), who agreed to participate in the study, were included. Exclusion criteria were patients with implantable cardiac devices who were decompensated or did not agree to participate in the study, unstable patients, or those with physical incapacity to perform the exercise test. Patients who did not complete phase II or had less than 80% of scheduled attendance were eliminated. All participants signed informed consent regarding the risks and complications of the test, as well as their entry into the CR program. Ethics, research, and biosafety regulations were complied with.

A treadmill exercise test was performed according to the Bruce or modified Naughton ramp protocol, limited by fatigue or absolute suspension criteria. VO2max, MET-max load were determined for all patients at the beginning and end of the CR program. After risk stratification and training prescription, the length of the program was determined based on physical capacity measured by achieved METs-load.

The training program consisted of concurrent exercise characterized by 3-5 days of dynamic exercise lasting 30 minutes, alternating treadmill with cycle ergometry, distributed as 5 minutes of warm-up, 20 minutes of exercise in the training zone at 65-80% of the reserve heart rate (RHR) calculated by the Karvonen formula, or between 60-80% of VO2max and by perceived exertion defined by Borg between 12-14, and 5 minutes of cool down. Strength training was performed at least two days a week, with a minimum duration of 20 minutes, and included flexibility, balance, and upper body strength exercises at 30-40% of 1RM and lower body at 40-50% of 1RM. Surveillance and control of cardiovascular risk factors were provided, as well as nutritional assessment, psychosocial care, and educational sessions on exercise techniques, occupational therapy, return to work, and smoking cessation techniques.

CI was analyzed by calculating the chronotropic response index using the formula (max HR - resting HR) / (220 - age - resting HR) with a normal value of 0.8, at the beginning and end of the program. For the purposes of this study, VO2max was determined during dynamic exercise in incremental load in a treadmill exercise test by obtaining the maximum achieved METs-load multiplied by 3.5 ml of O2/kg/min. VO2max = (number of METs X 3.5 ml of O2/kg/min).

STATISTICAL ANALYSIS

Forty patients were evaluated using the Shapiro-Wilk test to assess if the variables came from a population with a normal distribution. For the descriptive analysis of quantitative variables, the mean, standard deviation, and median were used, and for the description of nominal variables, percentages were used.

The comparison between before and after the intervention of the quantitative variables was performed with the Wilcoxon test, as it was a population with a non-parametric distribution. The correlation analysis between the dependent and independent variables was carried out using the Spearman statistical test. The SPSS® version 25 program was used for data analysis. Delta METs were obtained at the beginning and end of the intervention to determine the differences in gains between patients with normal CR and IC. Statistical significance was considered for values with $p < 0.05$.

RESULTS

A total of 58 patients were collected according to the inclusion criteria, of which 10 patients were excluded and 8 were eliminated for presenting one or more factors of the exclusion and elimination criteria respectively, leaving a final sample of 40 patients. The mean age was 61.4 years, mostly male (29) 72.5%, (23) 57.5% with a diagnosis of heart failure, and regarding the type of device, pacemakers (20) 50%, ICDs (12) 30%, and CRT-D (20) 8%, (Table 1).

TABLE 1.

Patient characteristics.	N (Media o %)
Age	61.45
Men	72.5%. (29)
Women	27.5% (11)
Diagnosing Heart Failure	57.5% (23)
Device type	
Pacemaker	50% (20)
ICD	30% (12)
ICD /CRT	20% (8)
Patients who required adjustment of device parameters	25% (10)
Use of beta-blocker	75% (30)
Type of HR response	
Chronotropic incompetence	87.5% (35)
Normal Chronotropic Response	12.5% (5)

Abbreviations: ICD: implantable cardiac defibrillator, CRT: cardiac resynchronization therapy HR: heart rate

Table 2 describes the characteristics of the exercise test pre and post-intervention, showing the differences (initial vs. final) in METs and chronotropic response index, where of the total patients, (35) 87.5% presented IC and only (5) 12.5% normal chronotropic response, finding a significant decrease in the chronotropic response index from 0.70 to 0.47 (p <0.001) and a significant increase in METs load from 5.47 to 9.35 (p <0.001).

TABLE 2.

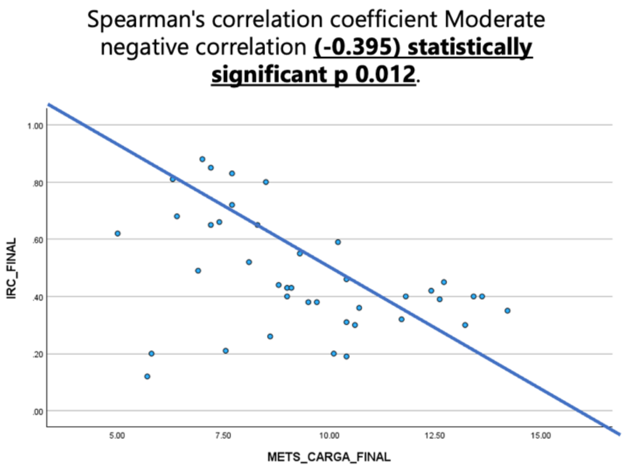
EVALUATION OF CHRONOTROPIC RESPONSE AND PRE- AND POST-PROGRAM LOADING METS IN PATIENTS WITH IMPLANTABLE CARDIAC DEVICES. (P <0.05)			
PARAMETER	INITIAL (n=40)	FINAL (n=40)	VALUE p
CHRONOTROPIC INDEX	0.70	0.47	<0.001
METS LOAD	5.47	9.35	<0.001

The differential value between initial and final METs (delta METs) was obtained for both groups, observing a statistically significant increase in METs gain (p=0.012) in patients with IC (3.8) compared to (3.5) in those with normal chronotropic response at the end of the intervention (Table 3). Finally, a moderate negative correlation was determined between IC and gain in exercise tolerance measured in METs of (-0.395) by Spearman method, statistically significant with a value (p=0.012) (Figure 1).

TABLE 3.

HR response type measured by chronotropic response index n=40	(Delta METs)
Chronotropic incompetence	3.8
Normal chronotropic response	3.5

FIGURE 1.



DISCUSSION

Our study addresses a fundamental aspect in the cardiac rehabilitation of patients with implantable cardiac devices (ICDs) with concurrent training on chronotropic competence. To begin with, a noteworthy aspect of our study is the inclusion of patients with different degrees of IC, suggesting that even those with a higher degree of incompetence can benefit from concurrent training. This is relevant as chronotropic incompetence was often considered a limitation for exercise in these patients [7], but our results suggest otherwise. According to our study, both types of training together can be beneficial for improving systolic volume in patients with ICDs, but aerobic training tends to produce greater improvements compared to resistance training [4]. This could be attributed to the more direct effect of aerobic training on the heart's ability to pump blood, in contrast to the more muscle-focused approach of resistance training. These findings are consistent with previous studies that have demonstrated the benefits of exercise in patients with ICDs [1, 2]. Furthermore, our study extends the evidence by showing that a comprehensive approach including different exercise modalities may be even more beneficial for improving functional capacity in these patients.

The linear relationship between oxygen consumption (VO2) and exercise intensity is well known, and similarly, cardiac output and frequency increase at the expense of that intensity.[22] The amount of muscle mass involved in the effort will directly determine oxygen consumption, but this will be dependent (to some extent) on the heart's ability to increase cardiac output.[23] This increase in cardiac output is mediated by multiple mechanisms: increased sympathetic tone, abolition of parasympathetic tone, feedback from mechanoreceptors and baroreceptors, production of metabolites, which simultaneously allow increased venous return, decreased peripheral vascular resistance, increased contractility and heart rate, which together determine a net increase in cardiac output and blood pressure, influencing the development of VO2. [24,25]

Long-term, intermittent hemodynamic overload creates necessary adaptations in the heart to better tolerate the generated stress: increase in the volume of cardiac cavities and wall thickness at the expense of an increase in the size of cardiac myocytes,[7] leading to an increase in stroke volume, decrease in heart rate at rest and submaximal efforts due to increased vagal tone, and improvement in myocardial perfusion[8]. On the other hand, VO2 depends on central and peripheral factors, with heart rate being a fundamental component for its increase, due to its effect on cardiac output generated by concurrent training, in patients with ICDs there is a limitation in the increase of heart rate, both due to the effect of the device itself, use of medications, and adaptations on heart rate due to training, which would initially lead us to think that the presence of CI in these patients would limit the gains in VO2 as supported by our hypothesis. However, our results contradict the hypothesis as it is shown that patients with ICDs undergoing a concurrent CR II program, showed a significant improvement in VO2 even over those with normal chronotropic response, which could be explained by the gains that concurrent training generates directly on stroke volume and DAVO2, and the effects of both on VO2, regardless of the degree of CI. [24,25] Other mechanisms implicit in this improvement could be the exerquins that play an important role in improving VO2, as they have direct cardiovascular benefits, for example, musclin increases mitochondrial biogenesis and cardiorespiratory fitness. The protein 1 similar to follistatin (FSTL1) improves endothelial cell function and promotes revascularization in ischemic tissue, apelin promotes vasodilation, increases myocardial contractility and angiogenesis, being these factors unrelated to heart rate that could contribute to the improvement of VO2 regardless of IC. [25,26,27]

These findings contradict the idea that CI is a barrier to improvement in this population, and suggest that the adaptations to physical training in patients with ICDs are similar to those of healthy populations and other cardiac patient populations.[1] Additionally, our findings support the evidence that exercise should not be prohibited in this population, but should be an integral part of their treatment to optimize their cardiovascular health and quality of life and thus obtain gains in exercise tolerance. [15,16,17,18]

Our study also adds to the existing literature by demonstrating that adaptations to physical training in patients with ICDs undergoing a concurrent cardiac rehabilitation program with prescription of aerobic exercise, strength training, and respiratory therapy are safe and effective for improving functional capacity, regardless of the degree of CI. [1,3,5,23] These findings have important implications for the design of cardiac rehabilitation programs and highlight the importance of exercise as an integral part of treatment in patients with ICDs.

Our results should be taken with caution due to the limitations of our study. Some of these include the relatively short duration of the training program and the limited sample size, as well as the lack of measurement of cardiorespiratory fitness through direct oxygen consumption; however, the use of METs load as a performance metric generates greater reproducibility in the vast majority of cardiac rehabilitation centers, due to the lack of expired gas analysis. These limitations could have affected our ability to detect significant differences in some results and make the interpretation of the effectiveness of the training program difficult [6, 8].

CONCLUSION

The results of this study suggest that, regardless of the degree of chronotropic incompetence, there is a significant improvement in exercise tolerance measured in METs load in patients with implantable cardiac devices after a CR II program. And that this improvement is attributable to the beneficial effects of a concurrent training program associated with respiratory therapy, on cardiac function, lung capacity, and peripheral circulation, where other factors and associated adaptations intervene. Although most patients included in the study had chronotropic incompetence, no significant association was found between this condition and exercise tolerance, rejecting the hypothesis that chronotropic incompetence limits improvement in exercise tolerance in this specific population of patients after a CR II program.

These findings are consistent with previous research showing that cardiac rehabilitation can improve functional capacity and quality of life in patients with heart failure and implantable cardiac devices, but emphasize that, regardless of the presence of CI, there will be gains in exercise tolerance, with important implications for the clinical management of these patients and opening a gap for future research to improve the prescription and management of this special population of patients.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethical Responsibilities

Protection of people and animals. The authors declare that no experiments were conducted on humans or animals for this research.

Data confidentiality.

The authors declare that no patient data appears in this article.

Right to privacy and informed consent.

The authors declare that no patient data appears in this article.

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