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Cardiovascular rehabilitation and exercise training programs in patients with heart failure

Programas de rehabilitación cardiovascular y entrenamiento físico en pacientes con insuficiencia cardíaca

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HEART FAILURE AS A PUBLIC HEALTH PROBLEM

Cardiovascular diseases are the leading cause of death worldwide, and over 80 million cases are expected for the year 2020[1]. Among them we have heart failure (HF), which is a clinical syndrome of complex presentation, resulting from various structural and functional changes that alter both the ejection of blood as the filling of ventricular chambers. The main manifestations of HF are dyspnea and fatigue that may limit exercise tolerance and cause fluid retention, pulmonary or splanchnic congestion and peripheral edema. In addition, patients usually have other problems such as arrhythmias, depression, fear, cachexia and a marked decrease or disappearance of sexual activity. Currently, the presentation of HF is classified, on the one hand, into that which is associated with a depressed left ventricular ejection fraction (LVEF) and, on the other, that which associated with a preserved LVEF[2].

HF is regarded as a public health problem worldwide due to its high incidence and prevalence, high mortality rate, close relationship with increasing age, high rate of hospitalizations, poor quality of life related to health (QLRH) and high health care costs[3].

The chance of suffering from HF at some moment in life is around 20%, and the incidence in highly industrialized countries, annually, account for more than 204 new cases per 100 000 inhabitants. On the other hand, the HF often becomes a chronic condition and a prevalence of about 5.1 million cases has been reported in Europe, where 2% of the adult population and over 10% of those over 70 years of age suffer from it[2].

Globally, and for several years already, a change in the distribution of population in different age groups with contraction pattern has been recognized, which particularly affects highly industrialized countries, as well as Eastern European countries and parts of Asia, a phenomenon known as epidemiological transition.

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There was an increase in the number of older adults with a decrease in the number of young people, with the consequent loss of the so-called demographic bonus. **Figure 1** shows this pattern in the French population census in 2005[4]

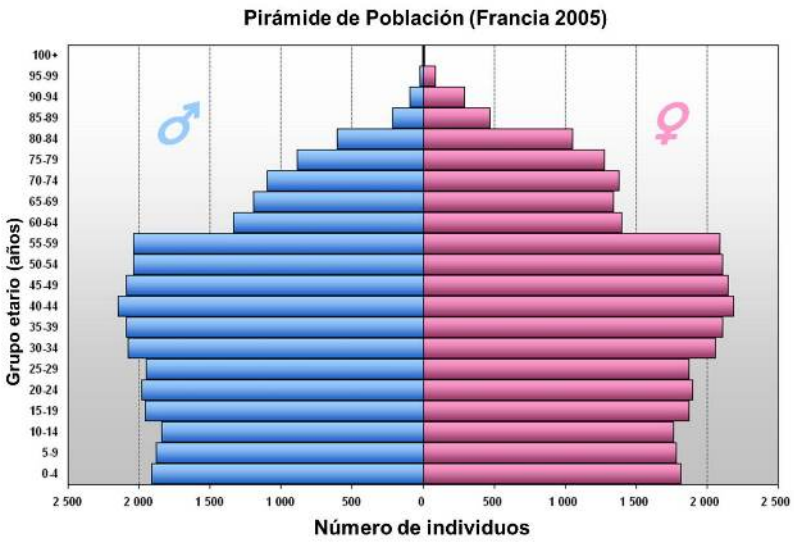

Figure 1. Epidemiological transition. This chart shows the age distribution of the French population in 2005. The contracted distribution pattern of this figure results from the sharp decline in young population (29 years and under), together with the increased number of individuals in the population between 30 and 60 years old. Modified: UN 2004[4].

The HF is a disease closely associated with age. The mortality rate in this group of patients is markedly higher than in those without HF[5]. The absolute mortality rate at 5 years after diagnosis is about 50%. Patients who were hospitalized for HF have a mortality rate of 10% within the first month, and 22% at one year after being discharged. Patients in an advanced stage of HF have a higher mortality rate at 5 years (80%) than those who are in the early stages (2-4%).

It has also been consistently reported the strong association between the presence of HF and a poor QLRH in these patients, particularly in women and in the areas of physical function and vitality. Furthermore, it has been noticed a higher mortality rate in patients who were discharged from the hospital for HF and had no improvement in their QLRH, turning this prognostic factor into a strong predictor of mortality in the medium and long term. In general, the therapeutic measures that have been associated with a better quality of life in patients with HF are cardiac resynchronization, self-care education and physical training programs. The last two interventions are essential components of the Cardiac Rehabilitation and Secondary Prevention Programs (CR-SPPs).

HF is one of the most prevalent causes of hospitalization, and leads to more than one million hospitalizations a year. Furthermore, the fact that a patient is discharged with a diagnosis of HF leads to a greater likelihood that he will readmitted in a span of a month (25%) or one year (83%)[2].

The QLRH in patients with HF is often comparable with other chronic conditions such as Parkinson's disease, certain neurological conditions or lung cancer[5]. However, observing the behavior of the QLRH in cancer patients after getting the diagnosis, it is noticed that these patients have a more or less stable QLRH until shortly before their death, when it deteriorates rapidly. In contrast, the deterioration of the QLRH in patients with HF begins long before death and takes place slowly and progressively, with the occurrence of some relapses followed by a partial recovery until death ensues, usually with a longer survival than cancer patients (**Figure 2**)[6].

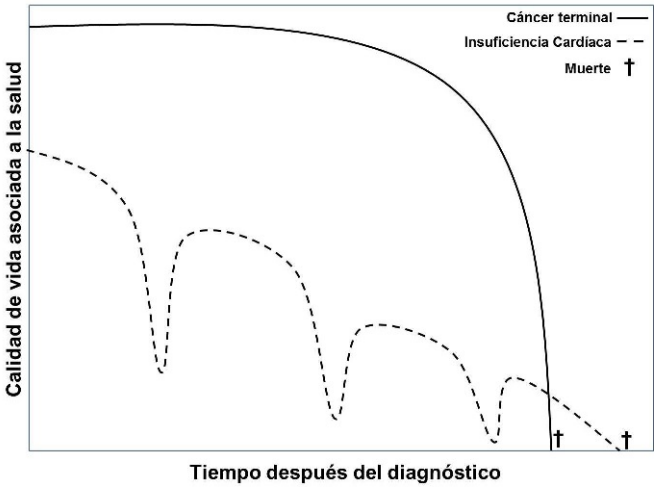

Figure 2. Comparison of quality of life in patients with heart failure and terminal cancer.

The health care costs of patients with HF amount to more than 20 000 USD a year per patient, which may become a load of billions of dollars for health services. This expenditure is mainly due to personal health care, medication and lost productivity.

CR-SPPs: EVIDENCE-BASED MEDICINE

Cardiac rehabilitation and secondary prevention integrate a medical program, initially based on supervised physical training, which aims to improve the health and wellbeing of people with cardiovascular disease. Currently, physical exercise is accompanied with a set of activities that make up a comprehensive intervention, including an educational program, detection and control of risk factors, and a continuous promotion of healthy cardiovascular habits[7].

The interest of the scientific community in the CR-SPPs has been growing in recent years and is reflected in the steady increase of publications on the topic. Currently, the number of articles on rehabilitation and heart failure which have been indexed in PubMed is close to 4 000, dated even in the 50s and 60s[8,9]. However, in the early 80s, the presence of HF was a contraindication to be included in a program of cardiac rehabilitation. At that time, patients were advised to have a prolonged rest, believing this prevented hemodynamic overload, arrhythmias and sudden death associated with physical activity. Years later, and based on several clinical trials, it was found that the physical capacity of patients do not have a strong association with the presence of low LVEF, and that peripheral determinants of exercise tolerance are the ones which have a substantial influence on the functional class and the QLRH of these patients.

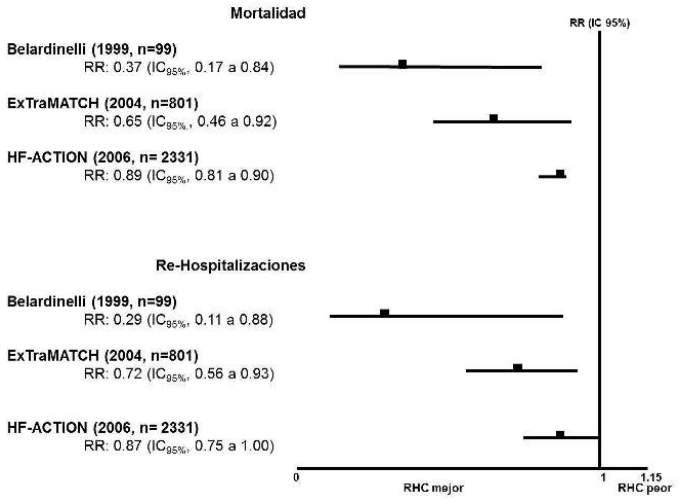

Figure 3. Long-term effect of exercise training on mortality and readmission rates in patients with HF. The therapeutic impact is shown as relative risk and confidence interval according to various published studies.

It has been shown that exercise training improves the working conditions of peripheral muscle in patients with HF, increases respiratory and endothelial functions, improves hemodynamic performance and reduces neurohormonal activation and inflammatory activity associated with HF[10]. Thus, at present, physical training in patients with HF is regarded as an effective and safe intervention, resulting in a class I-A recommendation, both by the European Society of Cardiology (ESC) and the American College of Cardiology (ACC)[1,2].

Physical training programs in patients with HF should be scientifically planned, as it is important to know the periods of overcompensation. If patients train intensely, on a daily basis, they do not give their body the necessary time to adapt and their exercise tolerance is increasingly worse. When planning a training program, it is necessary to use the moment in which the patient has gone through the period of recovery and is in the adaptation phase. The best performance is obtained when a new workload is administered at this time, about 48 hours after the first workload. Thus we can see how different studies show that this type of training improves 18%, on average, the exercise tolerance[10].

Several studies have been conducted to assess the effect of CR-SPPs in the survival of patients with HF. Belardinelli *et al*[11], in the early 90s, showed a clear decrease in mortality and in the incidence of readmissions at 5 years of follow-up in HF patients who were admitted to a physical training program (**Figure 3**). Similar results were observed in the ExTraMATCH study[12]. The HF-ACTION trial did not show, in the initial analysis, a statistically significant effect of physical exercise on mortality, but when the correction for demographic variables at 3 years of follow-up was carried out, a significant effect was noticed[13]. Besides the effect of the CR-SPPs in survival, a beneficial effect on the quality of life has also been noticed[14].

CR-SPPs: SCIENTIFIC PRODUCTION, RECOMMENDATIONS AND DISSEMINATION

Several groups of researchers around the world have conducted clinical trials, and various clinical practice

guidelines have been published (**Figure 4**). In the figure's planispheres, the global distribution of these scientific papers is observed, and the first thing that catches the eye is a marked imbalance in the production of original papers; most of them come from the European countries, USA, Brazil, Australia and Canada. Secondly, and something normal, the production of clinical practice guidelines on cardiac rehabilitation is lower, and these guidelines extend more to other countries that do not have a solid scientific production but which are interested in disseminating this information, especially in Latin America.

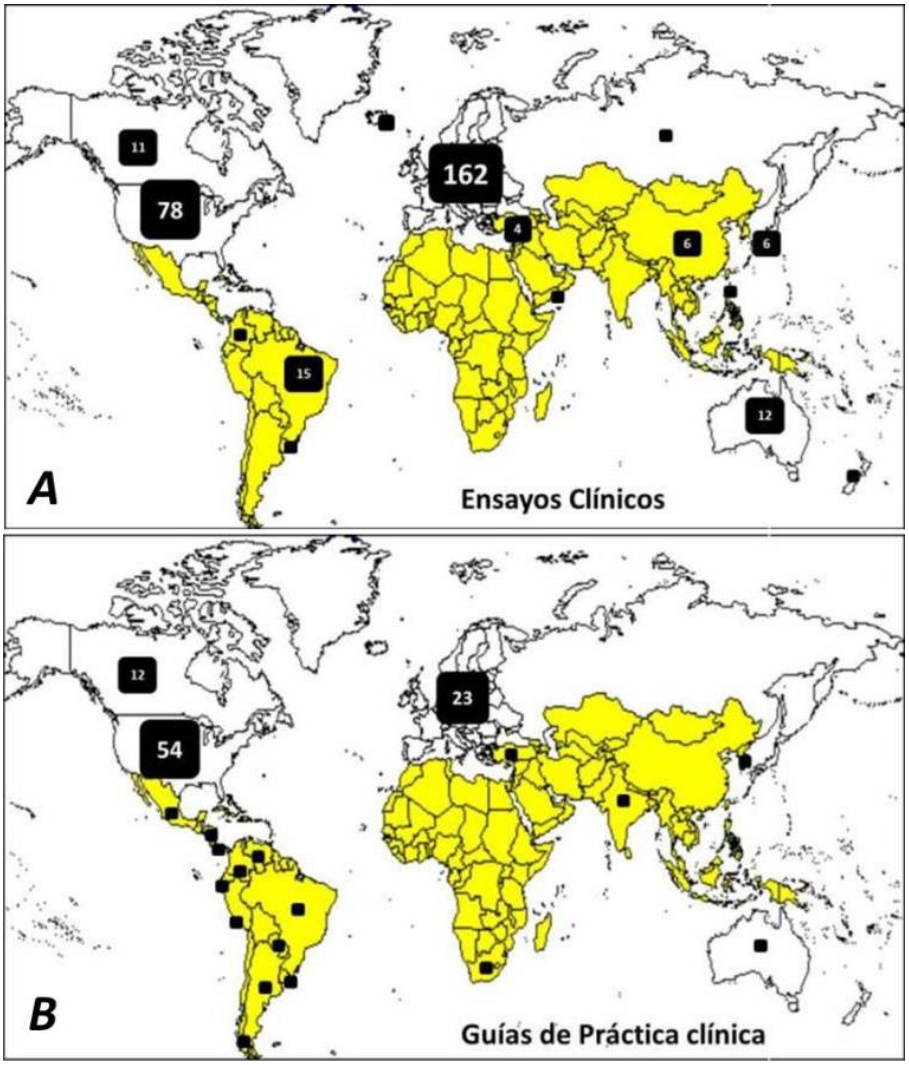

Figura 4. Global distribution of scientific production on Cardiac Rehabilitation Programs in HF patients, and its dissemination. **A.** Planisphere showing the original scientific production in the different countries of the world (Pubmed, June 2014). It is noticed that most of it is concentrated in the major centers of Europe, the USA and Asia. **B.** With regard to the publication of clinical practice guidelines, it is noticed that it substantially increases the participation of other countries, particularly in Latin America.

Recently, the main Societies of Cardiology (ACC, ESC) have published several guidelines for the care and treatment of patients with HF, where you can find many specific recommendations on the usefulness of the CR-SPPs[1,2]. In the ACC guidelines, the use of physical training in these patients is recommended to improve functional capacity (class I-A), plus improving the quality of life and reducing mortality (IIa-B). On the other hand, the control of risk factors for HF is also strongly recommended, for example, hypertension, dyslipidemia (I-A), diabetes, obesity and smoking (I-C). In a special section, counseling and patient education are also recommended to promote self-care (I-B). In the ESC guidelines, aerobic exercise is widely recommended (I-A) and a holistic treatment of these patients.

In terms of a cost-benefit balance of the CR-SPPs, several studies have been conducted in patients with ischemic heart disease, showing total savings ranging from 4 000 USD, during the first year, to some 100 thousand euros at 6 years per patient[15,16]. Thus, these therapies are not only useful in the clinical field, but also in the financial field, to the extent that insurance companies pay for CR-SPPs in patients with HF.

CR-SPPs: REAL USE

The problems caused by HF and the scientific evidence supporting the role of CR-SPPs in the treatment of these patients have been discussed above, including the recommendations by the main Cardiology Societies worldwide. However, facts are far away from the theory.

In the United States, despite having an important public health problem with HF and that its College of Cardiology strongly recommended the CR-SPPs, the percentage of target population that is referred to these programs re-

mains low. In 2007, 11% of patients with HF were referred to CR-SPPs, (OR = 0.77, 95% CI, 0.75 to 0.80), which was the lowest rate among the different cardiovascular diseases treated by these programs in USA[16].

A study by the Section of Cardiovascular Prevention and Rehabilitation of the European Society of Cardiology reported that the percentage of patients in a CR-SPP, that needed it, presented a median of 30% for stage II and 20% for stage III (**Figure 5**)[17]. In Europe, 53% of the associations that participate in this survey have clinical practice guidelines on Cardiac Rehabilitation, and 35% have some kind of document stating their position in this regard[18].

In contrast, there are some reports of other countries where the rate of referral and participation in CR-SPP is much higher. The National Cardiovascular Rehabilitation Program in Cuba declares a participation of 62.5% of patients with cardiovascular disease, which reaches 94.5% of patients after undergoing cardiovascular surgery[19]. Another example is Lithuania, where figures of referral to stage II are higher than 90%[18].

In Asia, though an accurate census is not available, it is recorded that in Hong Kong there are well-developed programs; however, the adoption of comprehensive cardiac rehabilitation programs is limited outside the West[20].

In Mexico, a census of cardiac rehabilitation centers was conducted in 2009, which reported a rate of referral to CR-SPPs of 5% in the states of Mexico that had at least one cardiac rehabilitation center. However, taking into account all the national territory, the rate of referral observed was lower than 0.6%. In Mexico, 35 position papers have been written, as well as 4 clinical practice guidelines on cardiac rehabilitation[21].

The fact that some patients do not get the benefits of being included in a CR-SPP is due to several causes, which can be divided into those barriers linked to the patient and those which are related to the health system. The main cause of this underutilization of cardiac rehabilitation is the low patient referral rate (which does not happen as a standard procedure) once they are discharged from hospital; and referral to specialized centers depends heavily on the knowledge and judgment of the doctor[22,23]. The characteristics of the doctor play an important role in increasing the referral of patients.

First, we must highlight the low adherence of doctors to clinical practice guidelines. A Dutch study showed that 30% of their doctors did not follow the recommendations of the guidelines. They argued that there was insufficient scientific evidence (68%), that there were serious organizational problems (50%), that they did not know the content of the guides (46%) or that the recommendations were ambiguous or unclear (43%)[24].

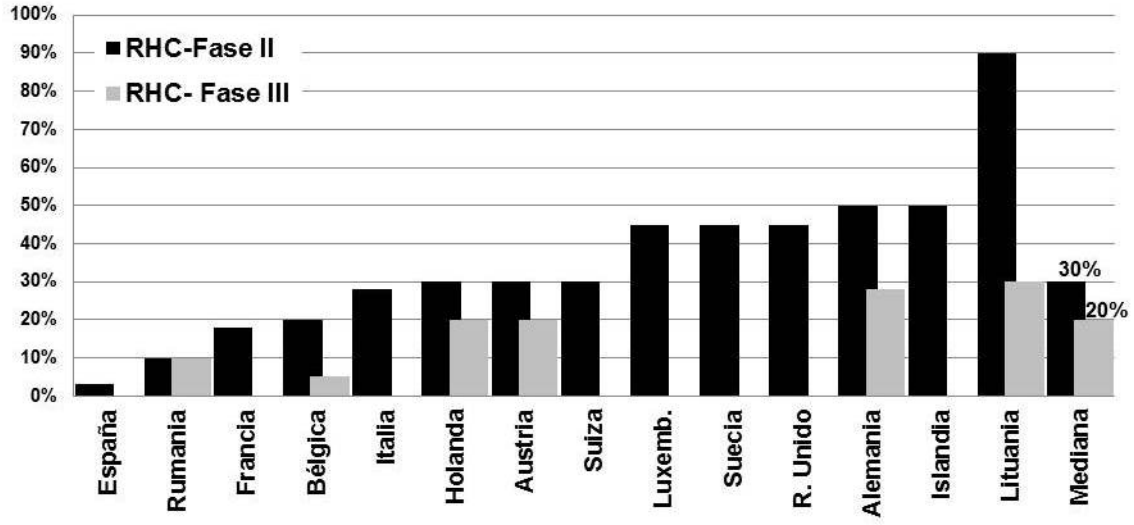

Figura 5. Percentage of patients that are referred to CR-SPPs in Europe. This chart shows the percentage of patients in Europe who were given a referral to CR-SPPs and were included in them. As can be seen the rate of referral is less than a third and most countries did not report the inclusion of patients in long-term programs (Phase III). Modified: Bjarnason-Wehrens B, *et al*. Eur J Cardiovasc Prev Rehabil. 2010;17:410-8[18].

With regard to the medical specialty, it has been noticed that when the patient is treated by a cardiologist or cardiac surgeon it increases several times the likelihood of being sent to a CR-SPP. On the other hand, male doctors are more likely to refer patients to CR-SPPs, compared with female health personnel[25]. The level of knowledge about the benefits and safety of these programs also has a significant influence[26]. Doctors found several obstacles to send their patients to CR-SPPs; for example geographic access, lack of patient motivation, the benefits reported in patients and not knowing the precise directions for referring them[27]. In another study, when doctors were asked about the cause for not referring patients to CR-SPPs, they said it was due to lack of coverage by insurance companies (50%), lack of patient motivation (40%), and 5% of them had some concern about the safety of the programs[28].

In short, the HF is an important public health problem worldwide and the care of patients who suffer from it is complex and multidisciplinary. The CR-SPPs have proved useful, safe and cost-effective in this group of patients, as they improve their exercise tolerance, functional status, quality of life and survival. The most important Societies of Cardiology in Europe and America advise the use of CR-SPPs for the treatment of patients with HF. These recommendations have been published in hundreds of scientific papers and dozens of clinical practice guidelines. Despite all this, CR-SPPs are frankly underutilized, regardless of the level of socioeconomic development of each country, which is due to many factors linked to both the patients and the health services.

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