**Abstract:** The development of implantable cardiac devices brought a spectacular improvement in the prognosis of patients with heart failure with reduced ejection fraction, reducing the risk of sudden cardiac death by implanting a cardiac defibrillator, improving ventricular remodeling through cardiac resynchronization and, at the same time, increasing the patient’s functional capacity, reducing decompensation episodes and hospitalization. Physical training at moderate exercise intensity is safe and effective in patients with heart failure and cardiac implantable devices; even if they have a severely impaired effort capacity and device-related issues, the assessment of the disease status and of the device parameters before the enrollment in the training program warrants the improvement of physical performance and disease outcomes without notable adverse events.

**Keywords:** physical rehabilitation; heart failure with reduced ejection fraction; cardiac implantable devices.

1. Introduction

The number of patients with heart failure and reduced ejection fraction (HFrEF) is steadily increasing [1] due to the effective drug treatment and interventional therapy of many heart conditions, which allows the overcoming of the acute phase complications. Even if the survival improves, the disease progresses however towards the final stage of heart failure when mortality and morbidity remains a considerable concern. At this stage, cardiovascular rehabilitation has proven its effectiveness in improving the prognosis and quality of life of the patients [2], even if not to the same extent as in patients with ischemic heart disease or those following cardiac surgery [3]. Thus, the ExTraMATCH collaborative group found a 35% lower risk for mortality and a 28% lower risk for the composite endpoint of mortality or hospitalization [4] for those patients following physical training programs.

HF-ACTION (Heart Failure – A Controlled Trial Investigating Outcomes of exercise TraiNing) enrolled 2331 patients with LVEF ≤ 35%, under optimal medical treatment, in the NYHA functional class II–IV. This study aimed to determine the safety and effects on the clinical status of a 36-session program of moderate-intensity training, followed by home-based training during a median follow-up time of 30 months [5]. In the training group, all-cause mortality and hospital stay were significantly reduced (by 11%).
Moreover, HF-ACTION confirmed the safety of exercise training in this patients category [6]. Similar encouraging results emerged from a larger meta-analysis as that of Taylor et al, which considered more than 4,700 patients and demonstrated no adverse events in the study arms following physical training [7].

The development of implantable cardiac devices also brought a spectacular improvement in the prognosis of these patients. Reducing the risk of sudden cardiac death by implanting the defibrillator, improving ventricular remodeling through cardiac resynchronization, and, at the same time, increasing the patient's functional capacity and reducing decompensation episodes and hospitalization are some of the benefits proven over 40 years since the first defibrillator implantation and 30 years of cardiac resynchronization therapy utilization. First trials were designed to assess the efficacy of the ICD therapy in reducing the sudden death risk in cardiac arrest survivors. Both MADIT [8] and MUSTT [9] enrolled patients with ischemic heart failure and LVEF below 35% and proved the benefits of ICD in cessation of sustained ventricular arrhythmia (VT and VF), also improving survival. The MADIT-II trial reported a 6.2% risk reduction in SCD with ICD versus medication (3.8% versus 10.0%) in patients with ischemic heart failure and LVEF less than 30% [10].

A few years later, in 2004, the DEFINITE trial extended the beneficial role of ICD in patients with nonischemic dilated cardiomyopathy. The risk of SCD in the ICD arm was 0.5 / 100 patient-years, 2.0 lower than in conventional therapy (2.5 / 100 patients/year), corresponding to a relative risk reduction (RRR) of 80% [11]. SCD-HeFT trial also demonstrated the efficacy of ICD for decreasing mortality by comparison with conventional therapy (RRR of 23%), in patients with ischemic and non-ischemic HFrEF and LVEF less than 35% [12]. Even if the DANISH trial did not demonstrate a benefit of ICD in preventing all-cause mortality in patients with nonischemic systolic heart failure, it does report a decrease of the SCD risk with ICD 0.7/ 100 patient-years [13].

All this solid evidence represents the background for the recommendations of cardiac resynchronization devices and, or implantable defibrillators use on an increasingly large scale. Thus, the incidence of patients with heart failure wearing implantable devices is still increasing. In the last decade, there has been a three-fold increase in the number of ICDs [14] and a 5-fold increase in the implantation of resynchronization devices [15]. It is expected that the increasing trend will continue, taking into account that, according to current recommendations, the number of candidates for CRT is 8-10 times higher than the number of implants that are performed [16]. Nowadays, in developed countries, the prevalence of implantable cardioverter defibrillator (ICD) carriers is 250/1,000,000/year [14] and respectively 100-200/1,000,000/year for cardiac resynchronization devices with/without defibrillator (CRT-D/CRT-P) [15]. According to some predictions, these encouraging data represent only 10% of the need for these devices in light of the current guidelines on device therapy in systolic HF [16].

As mentioned above, carriers of these devices are frequently encountered among patients addressed to rehabilitation programs, and the question in this situation is if the presence of the implantable cardiac device prohibits or makes it difficult to carry out the rehabilitation program.

From the cardiac rehabilitation point of view, the wearers of cardiac implantable devices could be grouped into three categories:

a. Implantable cardioverter defibrillator carriers
b. Cardiac resynchronization therapy patients with/without defibrillator
c. Patients with left ventricular assist devices, even if less numerous, but they can also benefit from attending physical rehabilitation programs.

**Particular issues of cardiac rehabilitation in implantable defibrillator carriers**

The implantable defibrillator increases the survival of patients with HFrEF as shown by aforementioned clinical trials [8,9,10,12], which demonstrated a reduction of up to 23%
in mortality with an NNT (number needed to treat) between 13 and 18, for both ischemic and non-ischemic heart failure.

Moreover, the ICD offers an even more consistent increase in survival among patients who have already survived a cardiac arrest (secondary prevention of sudden cardiac death). Thus, the meta-analysis of three trials (AVID, CASH, CIDS) reported a 28% reduction in the risk of sudden cardiac death among the survivors of a cardiac arrest (by VF or sustained TV) and those who were implanted with a defibrillator, compared to those treated with amiodarone only [17].

According to these benefits, the number of ICD carriers continues to increase and, as a consequence, it is expected that patients addressed to physical rehabilitation, encounter an increasing number of patients with heart failure and implantable defibrillators.

When addressed to physical rehabilitation, such a patient raises at least three issues:

1. Is patient safety jeopardized during training sessions?
2. What safety measures are recommended before the enrolment of an implantable defibrillator carrier in a physical rehabilitation program?
3. Are the benefits of physical rehabilitation preserved at this advanced stage of heart failure?

The implantable defibrillator does not jeopardize the safety of patients during physical training. The catecholamine stimulation during exercise is known to trigger rapid ventricular arrhythmias in patients with structural heart disease and increased arrhythmic risk. This is the case for implantable defibrillator carriers, and the question regarding the ventricular arrhythmia induction during the training sessions arises. Even if the presence of the defibrillator ensures a rapid intervention to cease the arrhythmia, this is still undesirable for at least two reasons: the success of the delivered therapies by the defibrillator is not entirely certain; even if it is validated as having a high success rate, this is not reaching the 100%, and secondly, even if not frequent, internal ICD shocks can have a significant unwanted emotional impact. A subanalysis of HF-ACTION trial showed no increase of the ventricular arrhythmic events in the active arm of the study (patients who attended the training sessions), neither during the 36 training sessions nor later, along the 4 years of follow-up [5], the total burden of internal shocks was also similar in both arms of the study (approximately 20% each group – standard medical therapy vs medical therapy and physical training) [6]. Defibrillator carriers accounted for a significant percentage in both arms, around 45%, with an average ejection fraction of 25%. The results of other smaller trials have also shown similar benefits of physical rehabilitation in terms of increasing effort capacity, improving quality of life and prognosis; no additional risk for arrhythmic events triggered by exertion was found. It should be noted that all patients enrolled in these trials were evaluated at the beginning of rehabilitation programs, through various monitoring methods, in terms of the arrhythmic burden and the efficacy of the recommended antiarrhythmic drugs.

Other concerns at the beginning of training sessions are those related to the behavior of the implantable defibrillator during effort and the complications that could occur:

a. broader chest movements may cause the dislodgement of the implanted device or leads [18];

b. increase in heart rate during exertion, either in the form of sinus tachycardia or supraventricular tachyarrhythmias; the paroxysmal ones, precipitated by effort, are rarer, more typical being represented by the high ventricular rate atrial fibrillation. All these supraventricular tachyarrhythmias can be misinterpreted as ventricular arrhythmias by the internal defibrillator, which will deliver inadequate therapy [19]; these events could have a demotivating effect on the patient, which will make a correlation between the effort and the unpleasant or even painful internal shock, leading to negative consequences regarding the willingness to engage further in physical activity [20].

c. the third issue that has to be considered is the risk of defibrillator malfunction, in terms of failure to detect ventricular arrhythmias that may occur during exercise [21], causing the arrhythmia to degenerate towards ventricular fibrillation and cardiac arrest.
This kind of complication is rare for current devices (more accurate in terms of detection algorithms by comparison with the first implanted models) and can be avoided by testing the parameters of the device before the start of the training program.

According to all these abovementioned issues, the European Association for Cardiovascular Prevention and Rehabilitation (EACPR) mentions some conditions that have to be met before the enrollment of a patient in a training program [22]:

1. Any training program should start at 6-12 weeks (on average at 8 weeks) after the implantation of the defibrillator when proving the stable fixation of the defibrillation lead at the endocardium level [23, 24] and the safety of its dynamic relation with neighboring structures (costoclavicular space, at which it can potentially be damaged by).

2. Checking the defibrillator lead parameters before enrolling in the training program. By measuring these parameters, one checks the lead’s integrity and proper fixation at the endocardial level. The 8-week time interval is considered enough to allow the definitivation of the endocardial scar that fixes the lead. Secondly, the internal memory of the defibrillator can store the ventricular arrhythmias episodes, and thereby provides an accurate follow-up about the efficacy of antiarrhythmic drugs and interventional procedures (myocardial revascularization, radiofrequency ablation) in terms of arrhythmia control.

3. If the endocavitary recordings of the heart rhythm stored by the implanted device are not conclusive, the assessment of the ventricular arrhythmic risk can also be performed by long-term recordings of the surface electrocardiogram (telemetry monitoring or ECG Holter). As is known from the general recommendations for cardiac rehabilitation, patients can be enrolled in a particular rehabilitation program if they do not have sustained rhythm disorders; moreover, they must have a well-controlled resting heart rate to allow training sessions. If these conditions are not met, training initiation should be delayed until an appropriate control of the ventricular rate is achieved by adjusting the antiarrhythmic drugs, serum electrolytes levels, or by interventional procedures.

4. The assessment of the patients with permanent or recurrent supraventricular tachyarrhythmias. Advanced heart failure is often associated with persistent or permanent atrial fibrillation. The presence of atrial fibrillation does not deny the initiation of training programs if the heart rate is well controlled [25]. This control is certified by telemetry, by Holter monitoring, or, in the case of dual-chamber implantable devices, by interrogation of their internal memory that also stores the supraventricular arrhythmia episodes, in terms of both the duration and the time of arrhythmia onset.

5. The heart rhythm and the heart rate behavior during exertion. Once control of the rhythm at rest is ensured, an exercise test limited by symptoms is recommended. It must be performed with the internal defibrillation function disabled and with an available external defibrillator. During the exercise test, several essential parameters are assessed because these will be used for the subsequent setup of the training program (blood pressure, heart rate, symptoms); from the implantable defibrillator point of view, the most important parameter is the maximum heart rate or the occurrence of ventricular/supraventricular arrhythmias. According to the aforementioned recommendations for cardiac rehabilitation, the occurrence of ventricular arrhythmia during exertion is a contraindication for the beginning of the training program. The maximum heart rate reached during exercise testing allows for the setup of the training heart rate [23]. At the same time, the detection “windows” of the defibrillator should be programmed 20-30 beats/minute above the maximum exercise heart rate to avoid the misinterpretation of sinus tachycardia as being ventricular arrhythmia and the delivery of inappropriate shocks by the defibrillator [19]. The detection “window” of the defibrillator is a heart rate range within which the device considers that a ventricular arrhythmia occurred.

6. Along with the programming of detection “windows”, some “pain-free” algorithms of the defibrillator were designed to facilitate exercise training by reducing the
risk of inappropriate shocks, even if, by accident, the training heart rate rises within the detection “window” of the device. By running these algorithms, the device will delay or even cancel the inappropriate internal shock [26,27]. Subsequently, the supervisor of the training session can reduce the intensity of the effort so that the heart rate falls below the detection “window” of the device.

The same document of EACPR provides some recommendations for the safety conduction of the training sessions to avoid device-related incidents [22].

1. The training must be designed considering those exercises with low traumatic risk in case of syncope. In this respect, it should be noted that exercises involving the mobilization of the left scapulohumeral joint (homolateral defibrillator pocket) are allowed, regardless of the amplitude of the movement, once the stability of the defibrillation lead has been tested two months after the implantation.

2. Continuous clinical surveillance and monitorisation of the heart rate should be provided during training, at least by digital pulse wave analyzers. If the patient has a higher arrhythmic risk (even for supraventricular arrhythmias), measures to avoid trauma should be provided in the event of (unlikely) arrhythmic syncope.

3. The duration of the training sessions is notably shorter and the intensity lower because the implantable defibrillator carriers have severely impaired left ventricle ejection fraction; after the first two weeks, the duration of the sessions can be progressively increased, followed by the possibility to increase the number of sessions per week and the intensity of the effort after that [28]. One can also introduce two sessions of endurance training per week to increase muscle mass.

4. Stable patients who did not encounter any of the aforementioned complications during the period of supervised training will receive recommendations for continuing physical activity at home concerning the functional status and individual possibilities of each patient (walking, running, cycling, recreational sports); the intensity of each activity will correlate with the level of effort reached at the end of the training program [29].

Patients with cardiac resynchronization devices

The LBBB in HFrEF results in interventricular and intraventricular contraction dysynchrony (between the posterior wall of the LV and interventricular septum), with additional hemodynamic impairment and remodeling of the left ventricle. Moreover, the subsequent worsening of mitral regurgitation, stroke volume decrease, and pulmonary hypertension are occurring. Cardiac resynchronization therapy, by inserting one pacing lead at the right ventricle apex and the second one at the lateral wall of the left ventricle, restores the synchronous electrical activation of the two areas and thereby restores the inter- and intraventricular synchronism [30]. Studies such as COMPANION and REVERSE have shown that in patients with LBBB and LVEF < 35%, resynchronization therapy improves LV volumes and hemodynamic profile and the hemodynamic profile [31,32], which translates into clinical benefits as improved functional capacity (NYHA class reduction, peakVO2 increase or longer distance achieved at the 6-minute walking test), reduction in hospitalizations, improvements in quality of life and survival (33). These benefits begin to validate three months after the resynchronization procedure and are fully validated after 6-12 months of resynchronization [31], because the substrate of all these benefits is the left ventricle revers-remodeling (improvement of diastolic volumes and stroke volume, increase of LVEF, reduction of mitral regurgitation) [32].

One raises the question of whether physical training prescription brings additional benefits in terms of aerobic performance in these patients already improved by resynchronization. Indeed, a sub-study of the COMPANION trial reported a 40% increase in peak VO2 in the group that combined CRT with 4 months of physical training compared to CRT alone, which led to an improvement of only 16% [33].
The particular issue in patients with CRT is represented by the need to maintain quasi-permanent bi-ventricular stimulation (of the interventricular septum and the lateral wall of the left ventricle) to avoid the relapse of the LBBB, delayed activation of the lateral wall and the consequences arising from it. As shown in the Guideline for Cardiac Pacing of the European Society of Cardiology, the benefits of resynchronization are lost when the percentage of biventricular pacing falls below 92% and are maximal at a biventricular pacing of more than 98% [30,35]. That is the rationale for maintaining biventricular pacing during exertion in CRT carriers. Optimal programming of the atrioventricular intervals of the pacemaker (shorter than the intrinsic PR interval, which normally shortens during the effort sympathetic activation that causes an increase in atrioventricular node conductivity) precludes the loss of biventricular pacing during effort.

These data represent a strong argument for the ECG exercise testing at the beginning of the rehabilitation programs in this patient’s category, with the monitoring of the atrioventricular interval, during effort and the preservation of the biventricular pacing throughout the whole exercise testing. Newer cardiac resynchronization devices are equipped with algorithms for automatic adjustment of the atrioventricular interval, so that the biventricular pacing is permanently ensured. Still, also, in patients carrying such advanced devices, the preservation of the biventricular stimulation must be documented by exercise testing.

Another parameter that has to be checked during the exercise testing is the heart rate adaptation to exercise for patients with chronotropic impairment.

Beyond these particularities, some of the patients with resynchronization therapy are carriers of much more complex devices (with dual function - resynchronization and defibrillation). Thus, the physical training will face additional “technical” issues already presented in the section on defibrillator carriers.

Patients with left ventricular assist devices

Initially designed for advanced heart failure patients, as an immediate, additional to medication, „short-term” treatment method (during critical decompensated episodes), or as a „bridge” (towards heart transplantation), left ventricular assist devices have become long-term cardiac support [36]. For continuous flow devices, survival is up to 80% per year and 70% every two years. The survival is altered if right ventricle dysfunction or renal failure are associated. By increasing portability, the newer devices offer increased feasibility during effort and thereby improve the quality of life [37]. For this reason, although scientific evidence is still limited [38], prescribing physical training would also be justified in these patients, once they are stabilized after the implantation, ensuring the functionality of the device during rest, and establishing the hemodynamic behavior during effort [39]. The optimal time to start training and the protocols to adapt the exercise to the device settings or patient comorbidities are being defined [40]. The European Society for Cardiovascular Prevention and Rehabilitation, however, provides some criteria for evaluating these patients before initiation of training, some recommendations for monitorization during training and for the evaluation after completion of the physical rehabilitation program [41].

Preliminary assessment

- medical history, prescribed medication
- clinical evaluation (focusing on signs of heart failure)
- the need for parenteral drugs or oxygen therapy
- vital signs, risk of hemodynamic or electrical instability
- neurological and cognitive status
- biological status: blood count, renal function, electrolyte balance;
- training can be started if: Hb > 9 g/dL, Na >130 mEq/L, K >3.8 mEq/L si Cr <1.9 mg/dL
Reducing the risk of adverse events during training

The items of the training sessions must be individualized:

- Prolonged warm-up and cool-down phases
- Mild exercise intensity, at most moderate
- Avoid deep breathing and Valsalva maneuver
- Avoid trauma, given the risk of the device damage and anticoagulant ± antiplatelet drugs
- Continuous ECG monitoring during training and 15 minutes after its completion
- Continuation of mobilization of the lower limbs during the cool-down phase

A scientific statement of the American Heart Association [42] defines the absolute and relative criteria for termination of exercise, which also apply in patients with heart failure and reduced ejection fraction that carry implantable cardiac devices:

**Absolute Indications**

- ST-segment elevation (>1.0 mm) in leads without preexisting Q waves because of prior MI (other than aVR, aVL, and V1)
- Drop in systolic blood pressure >10 mm Hg, despite an increase in workload, when accompanied by any other evidence of ischemia
- Moderate-to-severe angina
- Central nervous system symptoms (e.g., ataxia, dizziness, near syncope)
- Signs of poor perfusion (cyanosis or pallor)
- Sustained ventricular tachycardia (VT) or other arrhythmia, including second- or third-degree atrioventricular (AV) block, that interferes with normal maintenance of cardiac output during exercise
- Technical difficulties in monitoring the ECG or systolic blood pressure
- The subject’s request to stop

**Relative Indications**

- Marked ST displacement (horizontal or downsloping of >2 mm, measured 60 to 80 ms after the J point [the end of the QRS complex]) in a patient with suspected ischemia
- Drop in systolic blood pressure >10 mmHg (persistently below baseline) despite an increase in workload, in the absence of other evidence of ischemia
- Increasing chest pain
- Fatigue, shortness of breath, wheezing, leg cramps, or claudication
- Arrhythmias other than sustained VT, including multifocal ectopy, ventricular triplets, supraventricular tachycardia, and bradyarrhythmias that have the potential to become more complex or to interfere with hemodynamic stability
- Exaggerated hypertensive response (systolic blood pressure >250 mmHg or diastolic blood pressure >115 mmHg)
- Development of bundle-branch block that cannot immediately be distinguished from VT

**Contraindications for physical training**

- Heart rate > 100 beats/min (clinostat)
- O₂Sat < 90% (sometimes difficult to assess by pulse oximetry – weak/absent pulse wave)
- Complications related to the device during previous sessions - decreased device flow or decreased input flows - (warnings or alarms provided by the device according to data stored in its internal memory)
- Ventricular arrhythmias precipitated by effort or defibrillator interventions
- Infections or bleeding at the insertion site of the input/output of the device
5. Conclusions

Physical training at moderate exercise intensity is safe and effective in patients with heart failure and cardiac implantable devices; even if they have a severely impaired effort capacity and device-related issues, the assessment of the disease status and of the device parameters before the enrollment in the training program warrants the improvement of physical performance and disease outcomes without notable adverse events. Future research should design more accurate and individualized training protocols, which would translate into additional clinical benefits and increased cost-efficacy of the programs.


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