BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Physical rehabilitation in heart failure with reduced ejection fraction: are the cardiac implantable devices a barrier?

Gabriel Guşetu [1,2†], Bogdan Caloian [1,2,*], Raluca Tomoaia [1,2], Florina Frîngu [1,2,†], Lorena Mocanu [1], Diana Irimie [1,2], Horatiu Comşa [2], Gabriel Cismaru [1,2], Dumitru Zdrenghea [1,2], Dana Pop [1,2]

1 University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Romania;
2 Cardiology Department, Clinical Rehabilitation Hospital, Cluj-Napoca, Romania;

* Correspondence: Bogdan Caloian, email: bogdan912@yahoo.com
† These authors contributed equally to this work.

Citation: Guşetu G., Caloian B., Tomoaia R., Frîngu F., Mocanu L., Irimie D., Comşa H., Cismaru G., Zdrenghea D., Pop D. - Physical rehabilitation in heart failure with reduced ejection fraction: are the cardiac implantable devices a barrier? *Balneo and PRM Research Journal* **2023**, *14(4): 596*

Academic Editor(s): Constantin Munteanu

Reviewer Officer: Viorela Bembea

Production Officer: Camil Filimon

Received: 13.09.2023
Accepted: 04.12.2023
Published: 20.12.2023

Reviewers:
Mihail Hoteteu
Gabriela Dogaru

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

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 pa-tient's functional capacity, reducing decompensation episodes and hospitalization. Phys-ical training at moderate exercise intensity is safe and effective in patients with heart fail-ure 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 parame-ters 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 flollow-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 thr 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 conductibility) 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 adaption to exercise for patients with chronotropic impairment.

Beyond these particularities, some of the patients with resyncronization 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)
- O_2Sat < 90% (sometimes difficult to asses 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

- thrombotic complications of the device
- Weight gain > 1.8 kg over 2-3 days

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.

Author Contributions: Conceptualization, D.P. and D.Z. ; methodology, G.G., F.F. and G.C.; software, R.T. and D.I..; validation, F.F.; formal analysis, L.M.; investigation, H.C.; resources, G.G.; data curation, G.G., F.F. and B.C.; writing—G.G., F.F. and B.C.; writing—review and editing, D.P. and R.T.; visualization, D.I., H.C. and L.M.; supervision G.G., D.P. and D.Z.; project administration, G.G., F.F. and B.C.. All authors have read and agreed to the published version of the manuscript."

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Roger VL. Epidemiology of Heart Failure. Circulation Research. 2021;128(10):1421-34.
2. Tucker WJ, Beaudry RI, Liang Y, Clark AM, Tomczak CR, Nelson MD, et al. Meta-analysis of Exercise Training on Left Ventricular Ejection Fraction in Heart Failure with Reduced Ejection Fraction: A 10-year Update. Progress in cardiovascular diseases. 2019;62(2):163-71.
3. Swank AM, Horton J, Fleg JL, Fonarow GC, Keteyian S, Goldberg L, et al. Modest increase in peak VO2 is related to better clinical outcomes in chronic heart failure patients: results from heart failure and a controlled trial to investigate outcomes of exercise training. Circulation Heart failure. 2012;5(5):579-85.
4. ExTraMATCH Collaborative. Exercise training meta-analysis of trials in patients with chronic heart failure (ExTraMATCH). BMJ 2004;328:189–92
5. O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. JAMA. 2009;301(14):1439-50.
6. Piccini JP, Hellkamp AS, Whellan DJ, Ellis SJ, Keteyian SJ, Kraus WE, et al. Exercise training and implantable cardioverter-defibrillator shocks in patients with heart failure: results from HF-ACTION (Heart Failure and A Controlled Trial Investigating Outcomes of Exercise TraiNing). JACC Heart failure. 2013;1(2):142-8.
7. Taylor RS, Sagar VA, Davies EJ, et al. Exercise-based rehabilitation for heart failure. Cochrane Database Syst Rev 2014;(4):CD003331. https://doi.org/10.1002/14651858. CD003331.pub4; PMID: 24771460
8. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996;335:1933-40
9. Alfred E. Buxton, John D. Fisher, Mark E. Josephson, Kerry L. Lee, David B. Pryor, Eric N. Prystowsky, Michael B. Simson, Lorenzo DiCarlo, Debra S. Echt, Douglas Packer, G. Stephen Greer, Mario Talajic, the MUSTT Investigators, Prevention of sudden death in patients with coronary artery disease: The multicenter unsustained tachycardia trial (MUSTT). Progress in Cardiovascular Diseases 1993;36(3):215-226
10. Moss AJ, et al. "Prophylactic Implantation of a Defibrillator in Patients with Myocardial Infarction and Reduced Ejection Fraction". The New England Journal of Medicine 2002. 346(12):877-883

11. Kadish A, Dyer A, Daubert JP, Quigg R, Estes NAM, Anderson KP, et al. Prophylactic Defibrillator Implantation in Patients with Nonischemic Dilated Cardiomyopathy. New England Journal of Medicine. 2004;350(21):2151-8.
12. Poole JE, Olshansky B, Mark DB, Anderson J, Johnson G, Hellkamp AS, Davidson-Ray L, Fishbein DP, Boineau RE, Anstrom KJ, Reinhall PG, Packer DL, Lee KL, Bardy GH; SCD-HeFT Investigators. Long-Term Outcomes of Implantable Cardioverter-Defibrillator Therapy in the SCD-HeFT. J Am Coll Cardiol. 2020 Jul 28;76(4):405-415.
13. Wolff G, Lin Y, Karathanos A, Brockmeyer M, Wolters S, Nowak B, et al. Implantable cardioverter /defibrillators for primary prevention in dilated cardiomyopathy post-DANISH: an updated meta-analysis and systematic review of randomized controlled trials. Clinical Research in Cardiology. 2017;106(7):501-13.
14. Schmidt M, Pedersen SB, Farkas DK, Hjortshøj SP, Bøtker HE, Nielsen JC, et al. Thirteen-year nationwide trends in use of implantable cardioverter-defibrillators and subsequent long-term survival. Heart Rhythm. 2015;12(9):2018-27.
15. Hatala R, Lunati M, Calvi V, Favale S, Goncalvesová E, Haim M, et al. Clinical implementation of cardiac resynchronization therapy-regional disparities across selected ESC member countries. Annals of noninvasive electrocardiology : the official journal of the International Society for Holter and Noninvasive Electrocardiology, Inc. 2015;20(1):43-52.
16. Lee JH, Lee SR, Choi EK, Jeong J, Park HD, You SJ, et al. Temporal Trends of Cardiac Implantable Electronic Device Implantations: a Nationwide Population-based Study. Korean circulation journal. 2019;49(9):841-52.
17. Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck K-H, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. European Heart Journal. 2000;21(24):2071-8.
18. Fuertes B, Toquero J, Arroyo-Espliguero R, Lozano IF. Pacemaker lead displacement: mechanisms and management. Indian pacing and electrophysiology journal. 2003;3(4):231-8.
19. Guşetu G, Zdrenghea D. Urgente cardiace iatrogene. In: Zdrenghea D, (edt). Urgenţe cardiovasculare în camera de gardă. Cluj-Napoca: Clusium, 2019:220-57.
20. Lee KS, Kim JH, Kang KW, Miller J, McEvedy SM, Hwang SY, et al. Implantable Cardioverter Defibrillator Shocks and Psychological Distress: Examining the Mediating Roles of Implantable Cardioverter Defibrillator-Related Concerns and Perceived Control. The Journal of cardiovascular nursing. 2020;35(1):66-73.
21. Hauser RG, Kallinen L. Deaths associated with implantable cardioverter defibrillator failure and deactivation reported in the United States Food and Drug Administration Manufacturer and User Facility Device Experience Database. Heart Rhythm. 2004;1(4):399-405.
22. Isaksen K, Morken IM, Munk PS, Larsen AI. Exercise training and cardiac rehabilitation in patients with implantable cardioverter defibrillators: a review of current literature focusing on safety, effects of exercise training, and the psychological impact of programme participation. European journal of preventive cardiology. 2012;19(4):804-12.
23. Haennel RG. Exercise rehabilitation for chronic heart failure patients with cardiac device implants. Cardiopulmonary physical therapy journal. 2012;23(3):23-8.
24. Kiuchi MG, Schlaich MP, Ho JK, Carnagarin R, Villacorta H. Lifestyle advice for patients with ICDs: physical activity – what is healthy and what is contraindicated. E-Journal of Cardiology Practice [Internet]. 2019; 17. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-17/lifestyle-advice-for-patients-with-icds-physical-activity-what-is-healthy-and-what-is-contraindicated.
25. Cornelis J, Myers J, Heidbuchel H, Vrints C, Beckers P. Exercise Training in Heart Failure Patients With Persistent Atrial Fibrillation: a Practical Approach. Cardiac failure review. 2018;4(2):107-11.
26. Wathen M. Implantable cardioverter defibrillator shock reduction using new antitachycardia pacing therapies. American heart journal. 2007;153(4 Suppl):44-52.
27. Auricchio A, Schloss EJ, Kurita T, Meijer A, Gerritse B, Zweibel S, et al. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: PainFree SST trial primary results. Heart Rhythm. 2015;12(5):926-36.
28. Hansen D, Dendale P, Coninx K, Vanhees L, Piepoli MF, Niebauer J, et al. The European Association of Preventive Cardiology Exercise Prescription in Everyday Practice and Rehabilitative Training (EXPERT) tool: A digital training and decision support system for optimized exercise prescription in cardiovascular disease. Concept, definitions and construction methodology. European journal of preventive cardiology. 2017;24(10):1017-31.

29. Van Craenenbroeck EM. Exercise training as therapy for chronic heart failure. E-Journal of Cardiology Practice [Internet]. 2017; 14(43). Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-14/Exercise-training-as-therapy-for-chronic-heart-failure
30. M. Glikson et al. 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: Developed by the Task Force on cardiac pacing and cardiac resynchronization therapy of the European Society of Cardiology (ESC) With the special contribution of the European Heart Rhythm Association (EHRA), European Heart Journal 2021; 42(35):3427–3520
31. Salukhe TV, Francis DP, Sutton R. Co mparison of m edical therapy, p acing an d defibrillat ion in heart failure (COMPANION) trial terminated early; combined biventricular pacemaker-defibrillators reduce all-cause mortality and hospitalization. International journal of cardiology. 2003;87(2):119-20.
32. Linde C, Gold M, Abraham WT, Daubert J-C. Rationale and design of a randomized controlled trial to assess the safety and efficacy of cardiac resynchronization therapy in patients with asymptomatic left ventricular dysfunction with previous symptoms or mild heart failure—the REsynchronization reVErses Remodeling in Systolic left vEntricular dysfunction (REVERSE) study. American heart journal. 2006;151(2):288-94.
33. De Marco T, Wolfel E, Feldman AM, Lowes B, Higginbotham MB, Ghali JK, et al. Impact of cardiac resynchronization therapy on exercise performance, functional capacity, and quality of life in systolic heart failure with QRS prolongation: COMPANION trial sub-study. Journal of cardiac failure. 2008;14(1):9-18.
34. Daubert JC, Saxon L, Adamson PB, Auricchio A, Berger RD, Beshai JF, et al. 2012 EHRA/HRS expert consensus statement on cardiac resynchronization therapy in heart failure: implant and follow-up recommendations and management. Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology. 2012;14(9):1236-86.
35. Jin H, Gu M, Hua W, Fan XH, Niu HX, Ding LG, et al. Predictors of super-response to cardiac resynchronization therapy: the significance of heart failure medication, pre-implant left ventricular geometry and high percentage of biventricular pacing. Journal of geriatric cardiology : JGC. 2017;14(12):737-42.
36. Kirklin JK, Naftel DC, Kormos RL, Stevenson LW, Pagani FD, Miller MA, et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. The Journal of heart and lung transplantation : the official publication of the International Society for Heart Transplantation. 2013;32(2):141-56.
37. Adamopoulos S, Corra U, Laoutaris ID, Pistono M, Agostoni PG, Coats AJS, et al. Exercise training in patients with ventricular assist devices: a review of the evidence and practical advice. A position paper from the Committee on Exercise Physiology and Training and the Committee of Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2019;21(1):3-13.
38. Corrà U, Pistono M, Piepoli MF, Giannuzzi P. Ventricular assist device patients on the horizon of cardiovascular prevention and rehabilitation. Can we convert challenges into opportunities? European journal of preventive cardiology. 2012;19(3):490-3.
39. Fresiello L, Gross C, Jacobs S. Exercise physiology in left ventricular assist device patients: insights from hemodynamic simulations. Ann Cardiothorac Surg. 2021;10(3):339-352.
40. Bobenko A, Schoenrath F, Knierim JH, Friede T, Verheyen N, Mehra MR, Haykowsky M, Herrmann-Lingen C, Duvinage A, Pieske-Kraigher E, Halle M, Falk V, Pieske B, Edelmann F. Exercise training in patients with a left ventricular assist device (Ex-VAD): rationale and design of a multicentre, prospective, assessor-blinded, randomized, controlled trial. Eur J Heart Fail. 2019;21(9):1152-1159
41. Ambrosetti M, Abreu A, Corrà U, Davos CH, Hansen D, Frederix I, et al. Secondary prevention through comprehensive cardiovascular rehabilitation: From knowledge to implementation. 2020 update. A position paper from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. European journal of preventive cardiology. 2020: 2047487320913379.
42. Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, Coke LA, Fleg JL, Forman DE, Gerber TC, Gulati M, Madan K, Rhodes J, Thompson PD, Williams MA; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Nutrition, Physical Activity and Metabolism, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention. Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation. 2013 Aug 20;128(8):873-934. doi: 10.1161/CIR.0b013e31829b5b44. Epub 2013 Jul 22. PMID: 23877260.