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Exercise Training in Patients with Ventricular Assist Devices: A Review of the Evidences 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.

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Abbreviations

BiVAD	biventricular assist devices
CO	cardiac output
CPET	Cardiopulmonary exercise testing
EM	early mobilisation
ET	Exercise training
HF	heart failure
HFA	Heart Failure Association of the European Society of Cardiology
HT	heart transplantation
LV	left ventricle
LVAD	left ventricle assist device
peak VO_2	peak ventilator oxygen consumption
QoL	quality of life
VAD	ventricular assist device
VE/VCO ₂ slope	exertional ventilatory response
6MWT	6 minute walking test

Abstract

Exercise training (ET) and, secondary prevention measures in cardiovascular disease aim to favour early physical activity, to facilitate recovery and health behaviours. ET has been also proposed for heart failure patients with a ventricular assist device (VAD), to help recovery in functional capacity: cardiologists and health care providers are confronted with the need to resume daily life activities. However, the existing evidence in support of ET in these patients is still limited.

After review of the current knowledge on the origin of the limited exercise capacity, and on the benefit of ET in VAD patients, the Heart Failure Association of the ESC has developed the present document to provide practical advice on the modality to implement ET, beyond appropriate screening to avoid complications: starting from early mobilization, ET prescription is individualised to meet the individual patient's needs. Finally, gaps in knowledge are discussed.

Key words

Exercise training, left ventricular assist device, mechanical circulatory support, chronic heart failure.

Introduction

Around 5%-25% of heart failure (HF) patients present endstage condition, despite optimal medical therapy (1-2), when three options are currently indicated: ventricular assist device (VAD), heart transplantation (HT), or palliative care (3-4). In the modern setting of an increasing HF population and because of the scarcity of heart donors, the VAD option is emerging as a strategy for bridge to HT or as a destination therapy (DT) for those ineligible for HT (3): a small number of VAD patients may have sufficient recovery of myocardial function (bridge to recovery) to allow device to be explanted (4). Although, functional capacity usually improves compared to the pre-implantation status, VAD recipients still experience an impaired exercise capacity (5-6), and health care providers are confronted with the need to resume daily life activities for their patients.

Exercise training (ET) because of its beneficial effects on functional capacity and prognosis is highly recommended in HF (3, 8-10). More recently it has been proposed also in VAD recipients (11-12), but with a non-homogeneous implementation, as shown by the European Exercise Training Survey (13), attributed to lack of knowledge, prioritization, official recommendations, or heterogeneity of the surgical intervention (simple or shared device implantation, combined valve surgery, linked with ventricular ablation), indication (INTERMACS ranking), or simply because of too severe frailty individuals (such as elderly HF).

Based on the current consistent, but still limited evidences supporting the safety and the benefit of early mobilisation (EM) and ET in the VAD population, the Heart Failure Association (HFA) of the European Society of Cardiology has nurtured this document aimed at promoting the implementation of exercise in VAD patient in clinical practice. First the current knowledge on the origin of limitations in exercise capacity and the available evidences concerning the benefit of ET in VAD recipients are revised, thereafter advice on the modality to implement it in clinical practice are presented and, finally, the gaps in knowledge are discussed.

Exercise capacity in VAD recipients.

The transition from rest to exercise induces circulatory adjustments to allow adequate tissue perfusion as well as increased peripheral O₂ extraction. The normal physiologic response to exercise is characterised by increased heart rate and cardiac contraction force at a given left ventricular (LV) pressure, leading to higher cardiac output (CO), through activation of the sympathetic nervous system. During maximal exercise, CO normally increases 4- to 6-fold, shifting the Frank–Starling curve to the left and upward, associated with peripheral vasodilation (14). Although age, sex, fitness hereditary and the presence of congenital cardiovascular abnormalities might influence it, the ability to augment CO in response to the higher metabolic demand is one of the key factors regulating the cardiovascular response to exercise (14).

This situation is markedly different in individuals with heart disease, when coexistent demographic factors seem to be less critical (14). Usually, HF patients are limited in their exercise capacity by maladaptive changes in the cardiovascular, musculoskeletal, and respiratory systems (15-16). In particular in response to stress, advanced HF patients are unable to augment CO adequately due to impaired myocardial contractility, with consequent multi-organ under-perfusion, hypoxia and muscular inefficiency (17). Exercise limitation and deconditioning favour a negative loop (3).

Cardiopulmonary exercise testing (CPET) is considered the gold standard tool in assessing the physiologic response to

exercise (3, 18), and in identifying individuals in need of HT (18). Pre-implantation VAD patients may be too ill to perform it (4-5) and thus comparison of peak VO₂ values post implantation are mostly lacking (19-20) or showing conflicting results (21-23). Although the benefits of VAD support are unquestionable, patients still exhibit significant impairment in exercise capacity (6) in the post-acute phase, and several causes have been advocated:

- Device characteristics (e.g. inability to increase CO during exercise due to the absence of ramp function, unloading speed, the presence of the operating console and the drive line)
- Cardiac abnormalities (e.g. native LV contribution, right ventricular dysfunction, chronotropic incompetence)
- Co-morbidities (e.g. impaired pulmonary function, skeletal myopathy, endothelial dysfunction, anemia)
- Patient's characteristics (i.e. age, gender, disease aetiology and duration of disease, length of hospitalization and physical deconditioning).

Over long implant periods (i.e. 2 years), recipients show an enhanced exercise performance (24-25), either in terms of CPET parameters or 6-minute walking test (6MWT) (6, 19, 25-28).

LV unloading is important during VAD support (5), and as a result, device speed is adjusted accordingly. The pump flow is determined by the pump motor activity, the rotational speed, and the VAD characteristics (29), however, only poor estimation of the CO is possible because of the unknown volume of orthograde blood flow across the aortic valve, which is affected by residual LV myocardial function and pre- and afterload conditions. Rotational speed affects flow and exercise tolerance, as well (30-31), and speed increase affects exercise capacity and peak VO₂ (32-33)

After VAD implantation, the contribution of native ventricle contractility is complex: at rest, the VAD provides most of the CO, whereas, during exercise, variable contribution of the native heart to CO has been described depending on right and left contractile reserve interplay. (6, 27, 30). The role of heart rate seems less important (34), while right ventricle (RV) dysfunction may significantly limit CO max during exercise (33, 35-37): however tricuspid annular plane systolic excursion, a known marker of RV function, and RV diastolic dimension did not correlate with symptom-limited exercise capacity (34). Possibly, RV longitudinal strain, a less load dependent index of RV function, might represent a much more patho-physiologically relevant contributor to exercise capacity in a VAD patient, from the right side of the heart.

Finally the contribution of pulmonary function and peripheral factors are still unclear (35-37).

In conclusion, exercise adaptation of VAD recipient is hard to understand and curious: most studies have been focused on one limiting factor rather to describe exercise as a whole, therefore a complete description of exercise adjustment is not been worked-out, yet.

Review of the evidence for ET in VAD patients (Table 1)

Limited but promising data are available concerning the safety and the efficacy of early mobilisation (EM) (7 to 10 days post-implant) and ET in VAD patient (38-47). In 2011, Laoutaris et al (41) provided the first evidence on the feasibility and efficacy of ET in patients with either left ventricular (LVAD) or biventricular (BiVAD) assist devices participating to a 10-week exercise program, 6.3±4 months post-implantation. ET improved functional capacity (peak VO₂, 6MWT), exertional ventilatory response (VE/VCO₂ slope), and quality of life (QoL). Subsequently, Adamopoulos et al. (42) extended these findings, showing that long-term ET also decreased NT-proBNP and triggered myocardial growth factors involved in evolution signalling pathways, in both LVAD and BiVAD patients. A multi-model long-term (18 months) ET intervention increased percentage of predicted peak VO₂ in LVAD recipients (43), while a shorter (8-week)

ET, started early after implantation and on a small population (14 patients), provided no benefit with respect to the control group (44). In a retrospective analysis, Karapolat et al. (45) observed that an 8-week ET program improved peak VO_2 , pulmonary function and QoL similarly in LVAD recipients, HF or HT patients. Kerrigan et al. (46) in a 2:1 randomization trial comparing usual care versus ET (which included 18 aerobic exercise sessions at 60% to 80% of heart rate reserve), showed that ET improved exercise capacity (peak VO_2 by 10%, treadmill time by 3.1 min, 6MWT distance by 52.3 m), QoL (Kansas City Cardiomyopathy Questionnaire score by 14.4 points), and leg strength (17%). More recently, Marko et al. (47) confirmed the improvement in peak VO_2 and muscle strength in patients with LVAD after ET.

In conclusion, although the small studied population limits evidence regarding the role of ET in VAD recipients, all data support the feasibility, safety, and potential for benefit (39).

How to implement exercise

Based on the available data, the HFA Committees are putting forward the here presented practical advice on the modality of exercise implementation in VAD patients. However the reader should bear in mind that the followings are only general recommendations: the implementation in clinical practice is conditioned by local expertise, individual recipient's factor (e.g. timing of referral, type of intervention delivered, multidisciplinary approach), characteristics of the VAD recipients (e.g., combined vs. single surgical interventions, indications for implantation, underlying clinical condition, comorbidities), available national recommendation and facilities.

Preliminary step- clinical assessment and health professionals' education

Medical professionals may be hesitant to start mobilisation because of the presence of the device in a still debilitated patient, and specific skill and expertise are required.. Thus, the health care providers should be familiar not only with exercise physiology and the different exercise modalities but also with the functioning of the device (43), in order to face promptly all potential complications.

Full patients' history, clinical and functional evaluations are prerequisite as well as heart rate monitoring for detection and treatment of arrhythmias. Vital signs, self-reported scores, and VAD function should be monitored: in particular the mean arterial pressure in patients on non-pulsatile VAD support because hypertension would affect the VAD capacity to pump blood forward, while hypotension may lead to suction phenomena. The VAD team should be consulted if the mean pressure is below 70 mm Hg or higher than 90 mm Hg, especially when accompanied by VAD alarm activation. It is also important that the patient is well informed, reassured and feels safe and secure.

Exercise physiologist or physical therapist are responsible for putting in security the cannulas, drivelines and the VAD external equipment, to prevent damage during mobility (48-49). Once recipient is confident with transfers from bed, and shows the ability to carry and to manage the VAD, batteries, and controller (48), early mobilization (EM) can start. The external controller and batteries of last VAD generations are highly portable and do not significantly interfere with exercise activities, however, some attention should be directed to avoid abrupt posture changes and body balance issues that may result from carrying a bag, weighing from 2 to 2.5 kg. Complications such as disconnection from VAD's external power supply have been described (50-51). Table 2 provides instruction to reduce the risk of adverse events when exercising VAD patients, while table 3 lists the preliminary evaluation and precautions during EM.

Early mobilisation

In every patient, as well as in VAD recipients, EM, defined as initiating physical exercise within the early illness phase, is the first step for initiation of exercise therapy and it constitutes the basic standard modality for ET implementation, during the post-acute phase (Table 4); this preliminary phase is important but not standardised (52-53), as it is conditioned by the patient's status, facilities and referrals. Beside patient's needs, EM should be therefore adapted, and every day treatment changes should be considered: supervision from family members and/or nursing staff is warmly requested, to monitor VAD and clinical parameters

This phase is important to rule out contraindications to exercise (48) (Table 5) and should start only when troublesome accounts after VAD implantation are mostly over (50-51).

EM prevents the complications of muscle deconditioning and cachexia, and, through a broad range of activities, facilitates independency (53). EM favours ambulation and includes functional strengthening, muscle endurance and aerobic training, similarly to all other HF patients (54-57). Changes in gait are possible as result of earlier fatigue, appearance of new symptoms or unexpected VAD/clinical parameters changes. Possible falls and some complications as disconnection from the VAD's external power supply, due to the fact that the drive line has relatively short distance from the skin to the controller, have been described (50). The duration of EM is individualised according to the progresses and facilities (19, 50).

In conclusion, after VAD implantation, when patient's hemodynamic is stable (including surgical wound, skin integrity maintenance, and pulmonary hygiene), and VAD functioning and troubleshooting have been correctly directed (48, 50, 58), EM should be considered (54-56). As regards the timing of start, the limited data available are suggesting the safety of 6 weeks interval after implantation (59-60). An algorithm for EM for VAD-supported patients and the transition to ET is here proposed, based on expert opinion, and patient's aptitudes/clinical state (Figure 1).

Exercise training

No guidelines describing the specific ET setting, modality and duration for VAD-supported patients are available, but, as above described in Table 1, only limited evidences of implementation of light exercise intensities are available. A proper evaluation of symptoms and clinical signs, and echocardiography assessment may help in identifying most appropriate settings. Although it is reasonable to assume that longer ET interventions could improve physical fitness and QoL, the length and the long term adherence to these interventions has not been tackled yet. Monitoring of exercise sessions is, however, crucial at least initially, which include the supervision of the patient, the clinical adaptation, and the VAD functioning (48, 58).

To optimise exercise work-load prescription, a symptom-limited CPET (or 6MWT- according to local availability) is advisable (59), in order to aim at a peak work load below the predetermined ventilatory anaerobic threshold. If peak VO_2 is >14 ml/kg/min or 6MWT >300 meters, a more intensive exercise test can be considered. Figure 2 provides an algorithm for ET in VAD patients.

Currently, the most important issue is selecting the best VAD setting to obtain maximal CO, avoiding excessive emptying of the LV cavity and an inappropriate suction phenomenon on the interventricular septum. A careful evaluation of symptoms and signs, with echocardiography assessment may help in identifying most appropriate rotational speed adjustment. Additionally, caution is recommended to avoid excessive sweating and dehydration, as well as rapid changes of posture from supine to upright positions, which could reduce venous return and negatively impact VAD function (39, 48, 50, 58): patients should be urged to drink regularly.

Each single ET session starts with a warm up phase and is followed by cool down phase and includes conditioning and

endurance exercises: some exercise activities exert torsion on the drive line and might, therefore, must be avoided.

In summary, indicated exercises are: treadmill (increase ramp, not speed), static bike, hamstring curls in standing position, leg press, bicep curls, core stability, respiratory muscle training or arm ergometry. Contra-indicated ones are running, rowing machine, cross trainer, abdominals exercises, bilateral arms above head with weights or abduction with weights or swimming.

When to stop exercise

Exercise program should be stopped when:

1. New symptoms or signs are elicited (i.e. fainting, headache, shortness of breath, chest pain or thoracic pressure, fever, supraventricular or ventricular arrhythmias),
2. VAD alarms or related problems occur,
3. Unexpected changes in VAD parameters, i.e. flow, speed and watts operation.

Thus, monitoring of new signs and symptoms and VAD activity (alarms and related problems) during EM and ET sessions are needed, which can require to stop ET (Table 5). Of note, arrhythmias may appear during EM and ET: ventricular arrhythmias are frequent in VAD supported patients (61), due to a variety of causes (62-63). Sometimes, ventricular arrhythmias persist over time. Although “life-threatening” arrhythmias do not seem to be a major concern in recipients, since they provide modest hemodynamic deterioration, they should be carefully pondered as, if sustained, they might cause device dysfunction and might promote VAD-related symptoms. Before the prescription of specific anti-arrhythmic drugs, some proceedings should be considered: optimization of pharmacological therapy (fluid infusion and/or reduction of daily dose of diuretics), device setting change (if appropriate), and postural changes during exercise sessions (i.e. different sitting position during bicycle ergometer). When arrhythmias have been controlled at rest, exercise can be resumed, but at lower frequency and intensity and all exercise activities strictly supervised and ECG monitored. This is a cautionary attitude, not yet supported by scientific evidence. Atrial fibrillation occurrence may worsen symptoms and lead to deterioration of the patient’s clinical status, because of loss of atrio-ventricular synchrony and impaired ventricular filling: thus electrical cardioversion should be considered (62-63).

Thus, different factors should be considered when an exercise program is planned, in VAD recipients (39, 48, 50, 57-58, 64), as summarised in Table 6.

Gaps in knowledge

- a. The majority of studies so far have included mainly aerobic ET and data focused to different components of exercise physiology in VAD recipients are scarce. Thus the potential benefits of long-term alternative ET programs, such as resistance training, balance training and electrical muscle stimulation should be still investigated. Prolonged periods of ET are needed to observe significant effects in myocardial bioenergetics. This effect might be associated with unloading ventricles and better perfused organs by the VAD.
- b. The vast majority of the studies included only LVAD recipients, which highlights the need to investigate the benefit of ET in BiVAD patients.
- c. Studies comparing exercise capacity pre- and post- VAD implantation are lacking and might add understanding on the role of ET in these patients.
- d. Based on individual response and adaptation, EM usually starts early, few days after the intervention, while ET is

considered to continue indefinitely. However, the optimal timing and duration of each single ET session is not known yet.

- e. At the beginning, ECG and clinical monitoring are vital: for how long VAD recipients should be monitored is unknown, yet. Intuitively, more complicated VAD recipients need prolonged supervision.
- f. The most effective way to make a patient confident and feeling safe, and role of the caregiver have rarely been addressed. The potential beneficial contribution on patient education of a dedicated web-site needs to be investigated (66)
- g. The important role of CPET in the exact prescription of ET well established is advocated: unfortunately, CPET is poorly implemented, and the interpretation is unclear in VAD patients. In an ambiguous ground, anecdotal actions predominate, and therefore, for cautionary reasons, low intensity of aerobic training is here considered (50, 65-66).
- h. Arterial blood pressure is frequently indeterminable during ET or EM sessions; this is a limiting factor in monitoring EM and ET in VAD recipients. If detectable, measurement of blood pressure before and after exercise is useful, as excessive rise in blood pressure may induce adverse events like cerebral haemorrhage, stroke and pump thrombosis. Unfortunately, the blood pressure warning level is not unknown, yet; new symptoms due to exertional mal-adaptations and alert device-related problems (i.e. excessive work) should be considered as alarming signs.
- i. Ideally, ET may increase the possibility for a VAD to become a bridge-to-recovery, favouring the possibility of weaning, throughout the occurrence of metabolic changes in the failing myocardium and anabolic effects, together with the positive role an adjuvant pharmacotherapy (67-68). The activation of thyroid hormone signalling has been suggested to act as a biological driver for the up-regulation of physiological growth signalling pathways as indicated by the training-induced activation of the pro-survival signalling Akt and inactivation of the antihypertrophic JNK in cardiomyocytes, leading to physiological growth even in the failing myocardium. Anabolic pharmacotherapy (such as β_2 -adrenergic-receptor agonist clenbuterol) has been used to facilitate the myocardial recovery.
- j. VAD unloading therapy and ET might work together for the improvement of exercise capacity. Vignati et al. (32) showed that LVAD per se might improve exertional profile in recipients, independently of any ET approach. Only a randomized, non-exercising control group would be able to differentiate the improvements due to ET from those of device implantation.

Conclusions

Despite left ventricular unloading, impairments persist in VAD patients, with functional capacity frequently below 50% of predicted peak VO_2 . ET might provide additional benefit, but, today, there is little evidence. Actions should be taken in expanding our understanding on the potential role of ET therapy to promote its wider implementation in clinical practice.

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Conflict of interest

None

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Figure 1. VAD recipients and early mobilization

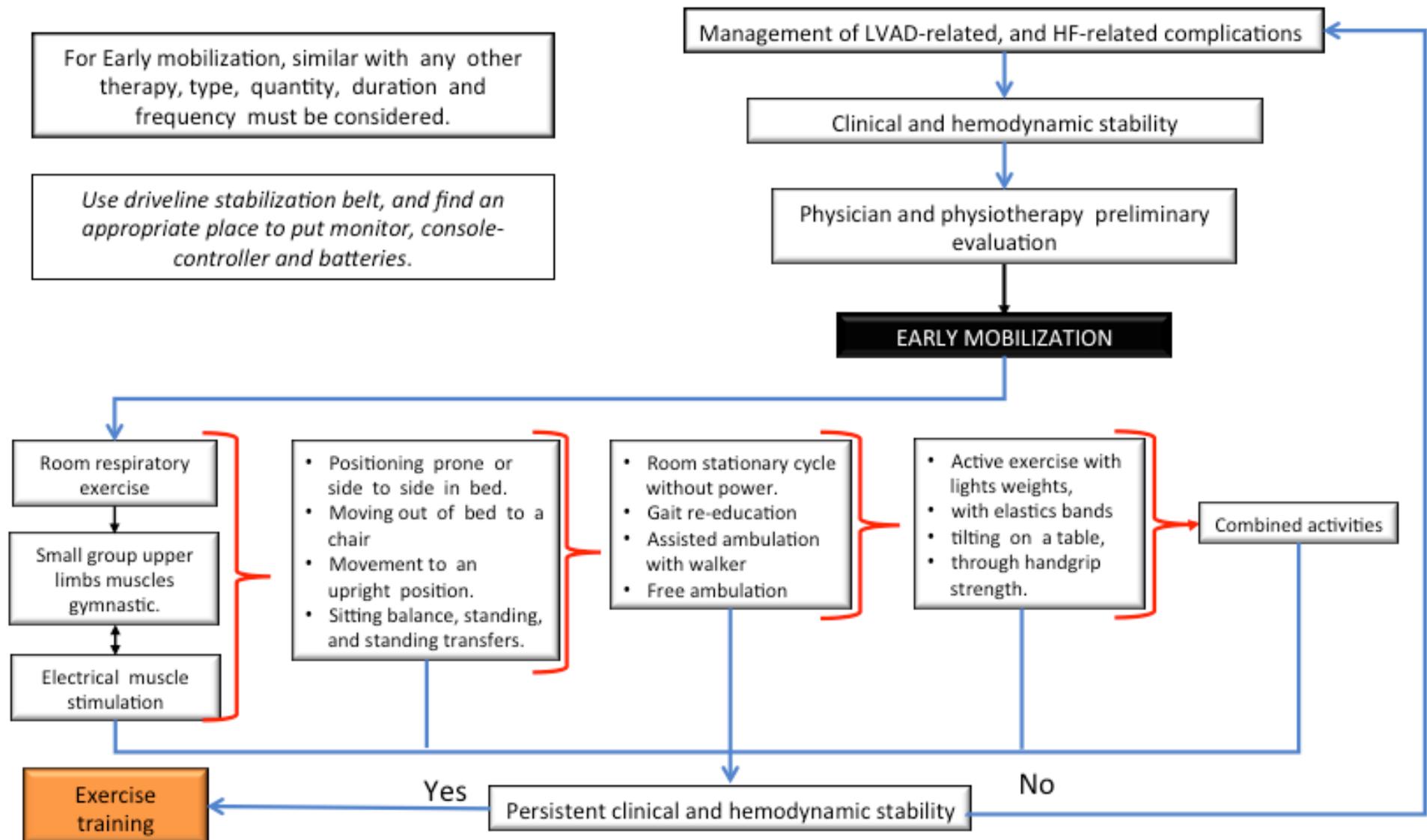


Figure 2. VAD recipients and exercise training

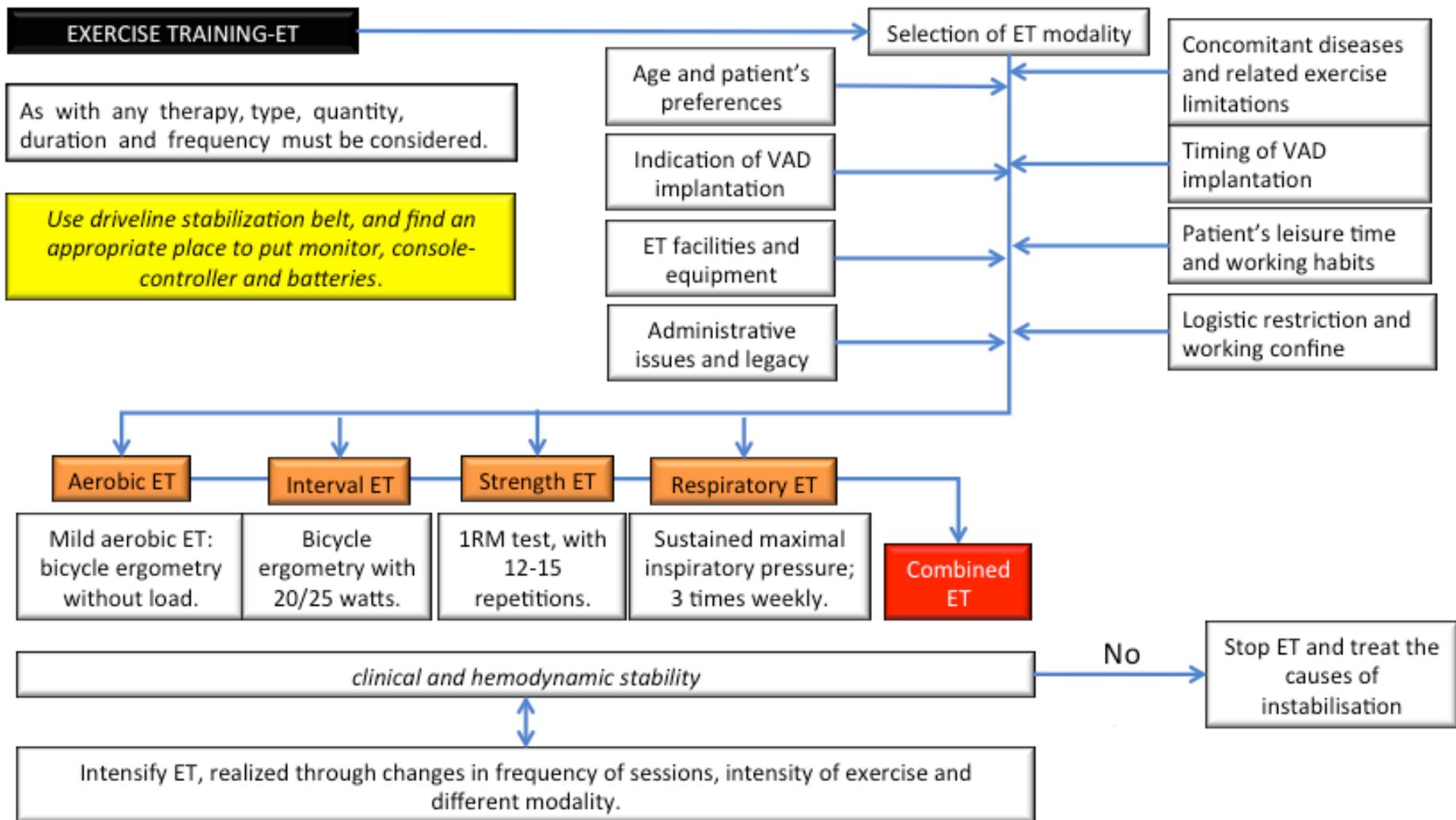


Table 1. Main studies on exercise training in cardiac rehabilitation of patients with ventricular assist devices

Study (year of publication), type of study	Type of recipients, and distribution in intervention and control groups	Time of enrolment after device implantation.	Type of intervention	Outcome's measurements
Laouratis 2011, <i>Randomized</i> (18)	<i>LVAD/BiVAD recipients</i> E =10, C =5 patients	After 6.3±4 months of device implantation	E: Home based, aerobic training, for 3-5 times/week. Supervised high intensity IMT for 3 times/week. Duration: 10 weeks C: Advice for walking	Improvement in peak VO ₂ , VE/VCO ₂ slope, 6MWT, QoL Inspiratory muscle function
Kugler 2012, <i>Non-randomized</i> (20)	<i>LVAD recipients</i> E=34,C=36 patients	After 6 weeks of device implantation	E: home aerobic training, dietary counselling and psychosocial support. Duration: 18 months C: No standard suggestion (only recommendation for healthy diet/routine exercise)	Improvement in peak VO ₂ (%pred.), QoL
Hayes 2012 <i>Randomized</i> (21)	<i>LVAD recipients</i> E=7, C=7 patients	Able to mobilize 70 meters	E: Supervised aerobic training, 3 times/wk. Strength exercise. Duration: 8 weeks. C: Advice for walking	Similar improvement in peak VO ₂ , 6mWT, QoL in both exercise and control
Karapolat 2013 <i>Retrospective and randomized</i> (22)	<i>LVAD recipients</i> E=11 patients compared to HF=46 and to HTx=40 patients	After 2.8±2.13 months of device implantation	E: Supervised flexibility, aerobic, strengthening, and relaxation exercises for 3 times/week. Duration: 8 weeks	Improvement in peak VO ₂ , QoL, depression scale.
Adamopoulos 2013 <i>Non-randomized</i> (19)	<i>LVAD/BiVAD recipients</i> E=11, C=11 patients	After 3 months of device implantation	Training up to HT E: Home-based aerobic training for 3-5 times/wk. Supervised high intensity IMT for 3 times/week. Duration: 10 weeks C: Advice for walking	Improvement in peak VO ₂ , NT-proBNP, T3, p-Akt/t-Akt p-JNK/t-JNK
Kerrigan 2014 <i>Randomized</i> (23)	<i>LVAD recipients</i> E=16, C=7 patients	Not available	E= supervised aerobic exercise, for 3 times/week Intensity= 60% of heart rate reserve. Duration: 6 weeks	Improvement in peak VO ₂ , treadmill time, 6mWT, QoL and leg strength.
Marko 2015 <i>Retrospective and non-randomized</i> (24)	<i>LVAD recipients</i> E=41 patients	After 48±34 days of device implantation	E: Supervised aerobic training/ strengthening/ walking/ gymnastics Duration: 32±6 days	Improvement in peak VO ₂ and muscle strength.

Abbreviations: LVAD, left ventricular assist device; BiVAD, biventricular assist device; IMT= inspiratory muscle training; E=exercise group; C= control group; HT,=heart transplantation; HF,=heart failure, Peak VO₂= peak oxygen consumption, VE/VCO₂ slope= ventilation vs carbon dioxide response to exercise, 6mWT=six minute walking test, QoL= quality of life.

Table 2. Instruction to reduce the risk of adverse events when exercising VAD patients.

1. Individualized assessment and prescription.
2. Pre-screening with risk stratification
3. Prolonged graduated warm-up and cool-down.
4. Low to moderate intensity exercise training.
5. Avoiding breath holding and Valsava manoeuvre.
6. Avoiding any trauma, as VAD recipients are anti-coagulated and (some, not all) treated with anti-platelet drugs.
7. Adaptation for comorbidities.
8. Monitoring and supervision.
9. Keeping the feet moving during active recovery, if appropriate.
10. Observation of patients for 15 min post cessation of exercise.

Table 3. Preliminary evaluation and precautions during early mobilization (EM) in VAD recipients.

1. Assessment.
 - a. recent and past medical history, and level of exercise capacity previous to disease state
 - b. mental status, and cognitive ability
 - c. vital signs and risk of cardiovascular instability (haemodynamic, arrhythmic, clinical)
 - d. medications, i.e. need for continuous or intermittent infusions (inotropic drugs), ventilator settings or oxygen requirements
 - e. screen range of motion, coordination, balance, strength, endurance, functional capacity (bed mobility, transfers, gait, daily living activities)
2. Follow sternotomy (6 weeks post-surgery screening of wound) and skin integrity.
3. Patients should always wear a driveline stabilization belt during exercise.
4. The patient should have his/her travel bag nearby at all times. It should include a back-up controller, battery clips and spare batteries.
5. Make early mobilization and exercise sessions comfortable. Organize an appropriate place to put monitor, console-controller and batteries (visible for patient and health care professionals). Discuss this topic with everybody implicated in the exercise program.
6. The VAD equipment location should not impede emergency procedures.

Table 4. How to set up an early mobilization program in VAD recipients**Consider**

1. positioning,
2. bed mobility activities,
3. sitting on edge of bed, in association with exercises,
4. transfers from bed to stretcher-chair, chair or commode.
5. gait, with pre-gait activities: weight shifting, stepping in place and sideways. Gait training is allowed with rolling walker.
6. breathlessness management and recovery strategies.
7. Attempt to achieve a target of 11 to 14 out of 20 of the Rate of Perceived Exertion scale.
8. Patient's native heart rate should not exceed 120 beats per minute during exercise, unless under physician's supervision: heart rate is not always detectable during early mobilization/exercise, and its monitoring depends on device.

Promote

- low to moderate intensity dynamic large muscle group work (e.g. walking, stationary cycling), or involving upper body muscles
- "walk & talk" approach is suggested.

Limit

- knee lifts
- resistance training (low weight/high repetitions) and with seated exercise (reduced venous return).

Avoid

- excessive muscle fatigue.
- abrupt postural changes and stooped activities.
- rowing machine.
- Initially, biking due to increased risk of infection near VAD percutaneous line exit site.

Table 5. Criteria for exercise contraindications in VAD recipients.

1. Symptoms and signs compatible with exercise intolerance including light headedness, severe-intolerable dyspnea, chest pain or discomfort, tachycardia and exaggerated blood pressure response.
2. Symptomatic hypotension (fainting, dizziness, or diaphoresis, as extreme fatigue or claudication and new onset of neurological changes).
3. Supine resting heart rate >100 beats per minute.
4. Oxygen saturation < 90%. (caveat: oxymetry readings might be difficult to obtain due to low pulsatility)
5. VAD complications during or after exercise sessions:
 - a. Alarm activation Curves, numbers and alarms should be displayed on the VAD monitor: trends are useful to track pump function and patient perfusion. Significant drop in LVAD flow, or suction alarm are criteria for interrupting the session.
 - b. Complex and frequent ventricular arrhythmia on exertion (Caveat: *may be asymptomatic*)
 - c. Infection, mainly at the driveline site. (Infection control procedures should be followed at all times, e.g. cleaning of the equipment, hand washing, disposal of sharps.
 - d. Evidence of bleeding as VAD recipients are anti-coagulated or treated with anti-platelet drugs (not all): these drugs are essential for device working, but they can also enhance exercise-related bleedings and hematomas.
 - e. Thrombus (usually evidenced by an increase in the number of watts/energy necessary for device working).
6. Request of VAD recipient to stop.
7. Increase >1.8 kg in body mass over the previous 1 to 3 days.
8. Implantable cardioverter defibrillator intervention (anti-tachycardia pacing and shocks)

Table 6. Summary of clinical parameters to be considered when exercising in VAD patients

clinical stability	Early mobilization	Functional capacity	Exercise training
<ul style="list-style-type: none"> unchanged VAD parameters, complication VAD-related and not-related appropriately tackled 	<ul style="list-style-type: none"> Duration of EM according to patient's condition, VAD parameters, co-morbidities and complications According to institutional administrative legacy, but max duration of six weeks is suggested 	<ul style="list-style-type: none"> Preliminary assessment by Cardiopulmonary exercise testing (CPET) or 6 min Walk Test (6MWT) 	<ul style="list-style-type: none"> Duration of ET according to patient's condition, VAD parameters, co-morbidities and complications According to institutional administrative legacy: Setting: in- or outpatient approach
<p><i>Clinical stability, ie</i></p> <ul style="list-style-type: none"> Stable diuresis Stable weight No ECG changes No complex and/or sustained ventricular arrhythmias No new sustained supraventricular arrhythmias No changes in mean blood pressure (< 60 mmHg or > 100 mmHg) <p><i>and no device failure</i></p> <ul style="list-style-type: none"> No flow less than 3L/min No suction events No device alarms <p><i>and concomitant disease addressed</i></p> <ul style="list-style-type: none"> No Thrombosis-Hemorrhage No Infection No Right ventricle failure No Lung, liver and kidney failure No Neurological problems 	<ul style="list-style-type: none"> Mean while management of acute care factors including surgical wound, skin integrity maintenance, pulmonary hygiene, a range of motion, cardiovascular, and muscle strength maintenance should be addressed with the goal of free ambulation. The cannulas, drivelines and the VAD external equipment must be secure to prevent damage during mobility and attention should be directed to abrupt posture changes and body balance issues that may result from carrying a bag, and might lead to disconnection of VAD. 	<ul style="list-style-type: none"> CPET: progressive ramp protocol is recommended, starting with a warm-up 0 W phase, following a ramp protocol of 1 min steps of 10 W/min.), aiming subjective exhaustion or appearance of criteria for interruption. 6MWT: should be performed indoors, along a long, flat, straight, enclosed corridor with a hard surface that is seldom traveled. The walking course must be 30 m in length. The turnaround points should be marked and a starting line, which marks the beginning and end of each 60-m lap, should be marked on the floor. Only standardized phrases for encouragement must be used during the test. 	<ul style="list-style-type: none"> Light exercise intensities is recommended, with monitoring of exercise sessions. If peak VO₂ > 14 ml/kg/min, or >300 meters are ambulated at 6MWT, a more intensive exercise session might be prescribed.