

ACCEPTED: March 2015

PUBLISHED ONLINE: April 2015

DOI: 10.5960/dzsm.2015.176

Egger A, Eichinger J, Oberreiter H, Humphrey R, Niebauer J. Exercise training as effective therapy for a patient with left ventricular assist device. 2015; 66: 104-108.

Exercise training as effective therapy for a patient with left ventricular assist device

Training als effektive Therapie für einen Patienten mit Links-Herz-Unterstützungssystem

1. PARACELSUS MEDICAL UNIVERSITY SALZBURG, Salzburg, Austria
2. THE UNIVERSITY OF MONTANA, School of Physical Therapy & Rehabilitation Science, Missoula, MT, USA

Summary

- › **In this case report**, we describe the effects of an outpatient cardiac rehabilitation program that was supplemented by unsupervised home-based exercise training in a patient with a left ventricular assist device (LVAD). This patient performed cycle ergometer as well as resistance training once weekly for 9 months in our outpatient cardiac rehabilitation program and supplemented his home-training as recommended by us with 6 Theraband exercises of 15 repetitions each, at least three days a week. What is unique about this case is the complex clinical status of the patient and his responses with just one supervised training session per week. Since, amongst others, exercise power (Pmax) and quality of life (QOL) improved, this suggests that other compliant patients with VADs may also benefit from an outpatient rehabilitation program, which would decrease resource allocation.
- › **Furthermore**, combined endurance and resistance exercise training were found to be safe in this case and led to an improvement in Pmax and only a subtle decline in his psychosocial status, which may have been worse without outpatient cardiac rehabilitation as observed in other very ill patients.
- › **We could demonstrate** that even an LVAD patient can benefit from outpatient cardiac rehabilitation and may eventually be weaned off close supervision. Even though response to rehabilitation will be very individual, especially in these patients, colleagues might feel encouraged by our report to also consider teaching LVAD patients about outpatient cardiac rehabilitation and eventually home-based exercise training.

Zusammenfassung

- › **In diesem Fallbericht** beschreiben wir die Auswirkungen eines ambulanten kardiologischen Rehabilitationsprogrammes bei einem Patienten mit einem Links-Herz-Unterstützungssystem (left ventricular assist device, LVAD), welches von zu Hause aus mit einem unbeaufsichtigtem Bewegungstraining ergänzt wurde. Dieser Patient trainierte einmal wöchentlich für 9 Monate in unserer ambulanten kardiologischen Rehabilitation und ergänzte sein Trainingsprogramm zu Hause mit Therabandübungen, die er für 6 Muskelgruppen mit je 15 Wiederholungen an mindestens drei Tagen in der Woche durchführte. Das Besondere an diesem Fall ist der komplexe klinische Zustand des Patienten und seine Reaktionen mit nur einer betreuten Trainingseinheit pro Woche. Da sich unter anderem die körperliche Leistungsfähigkeit und die Lebensqualität (LQ) verbesserten, bedeutet dies, dass auch andere Patienten mit LVAD von einem ambulanten Rehabilitationsprogramm profitieren könnten und so weniger Ressourcen aufgebracht werden müssten.
- › **Darüber hinaus** scheint kombiniertes Ausdauer- und Krafttraining in diesem Fall sicher zu sein und zu einer Verbesserung der körperlichen Leistungsfähigkeit zu führen, mit nur einem subtilen Rückgang im psychosozialen Status, welcher noch schlechter gewesen wäre ohne der ambulanten kardiologischen Rehabilitation.
- › **Wir konnten zeigen**, wie ein Patient mit LVAD von der ambulanten kardiologischen Rehabilitation profitierte. Auch gelang es ihm ohne Aufsicht zu Hause trainieren zu lassen. Wenngleich der Rehabilitationsverlauf solch komplexer Patienten sehr individuell ist, so sollte aufgezeigt werden, dass es sehr wohl möglich ist, solche Patienten von der engen Betreuung während der ambulanten kardiologischen Rehabilitation zu entwöhnen und ihnen ein Heimtraining zu ermöglichen.

KEY WORDS:

Cardiovascular disease, endurance- and resistance training, physical work capacity, heart failure, Thoratec Heartmate II

SCHLÜSSELWÖRTER:

Herz-Kreislauferkrankungen, Ausdauer- und Krafttraining, körperliche Leistungsfähigkeit, Herzinsuffizienz, Thoratec Heartmate II

Introduction and purpose

Outpatient cardiac rehabilitation provides significant benefit to patients with cardiovascular disease (CVD) and this is manifested in clinical as well as health-related endpoints including cardiovascular and all-cause mortality (11). As a result, exercise training has been included in current European recommendations and guidelines as an evidence-based therapeutic option (24,25). Nevertheless, patients

with severely compromised ventricular function and especially those with a left ventricular assist device (LVAD) pose quite a challenge to cardiac rehabilitation. Mechanical devices have evolved since research initiated in the late 1970's and early 1980's (10); evidence of VADS traces to the early 1990's (28). Expected physiological responses to exercise were described by Humphrey et al. in 1997 (12) and the first



QR-Code scannen und Artikel online lesen.

CORRESPONDING AUTHOR:

Professor Josef Niebauer, MD PhD MBA
Paracelsus Medical University Salzburg
Lindhofstraße 20, 5020 Salzburg, Austria
✉: j.niebauer@salk.at

set of clinical guidelines appeared in 1999 (2), with a subsequent update in 2003 (14). As described by O'Connor et al., exercise training appears to be both safe and effective in improving a variety of parameters in this patient population (22), although more published data is needed, given the variety of devices and the intent of the devices in patients, be it as a bridge to heart transplantation (HTX), or as a destination therapy.

There is limited literature describing exercise training in patients with LVADs in European cardiac rehabilitation programs. The purpose of this case report is to describe the effects of supervised as well as unsupervised exercise training on maximal exercise capacity and quality of life (QOL) in a patient with an LVAD.

Case Description

The patient is a 49 year old male from the state of Salzburg in Austria. In June 2010, he received an LVAD-Thoratec HeartMate II due to ischemic heart failure, which was first diagnosed in 2005, and underwent simultaneous reconstruction of the tricuspid valve (32mm Edwards MC3 ring). He had undergone implantation of an automated defibrillator (ICD) in July 2008, following an episode of syncope and ventricular fibrillation. The patient was treated with all medical options including medication and interventional therapy. Prospects of a long waiting time for an available organ was the primary reason for LVAD implantation as a bridge to HTX. Thoratec HeartMate II is designed to supplement the pumping function of the heart. The device is placed just below the diaphragm in the abdomen. Its inlet is attached to the left ventricle and its outlet connected to the aorta. Blood flows from the heart into the pump. A small electric motor in the pump drives a rotor (similar to a propeller) inside the pump that provides continuous blood flow into the aorta and out to the body. A flexible tube passes through the patient's skin and connects the implanted pump to a small controller (powered by batteries) worn under or on top of clothing (figure 1).

The patient was in a severe stage of heart failure before receiving his device, he was very debilitated and very limited in terms of activity level. After receiving HeartMate II, he was more able to return to his favorite daily activities, with the primary limitation being water immersion. Following LVAD implantation, physiotherapists performed easy range of motion exercises for better recovery while the patient was still treated in our department of cardiac surgery.

After written consent was obtained and all testing was completed, cardiac rehabilitation was initiated within one week after referral. Patient's medications at enrollment and discharge from cardiac rehabilitation are listed in table 1.

Baseline patient assessment

Clinical examination: On examination, the patient (height: 179.1 cm; weight: 97.5 kg; BMI 30.3) appeared physically compromised and his vital signs included a regular heart rate of 60 beats per minute, blood pressure of 100/60 mm Hg, and an

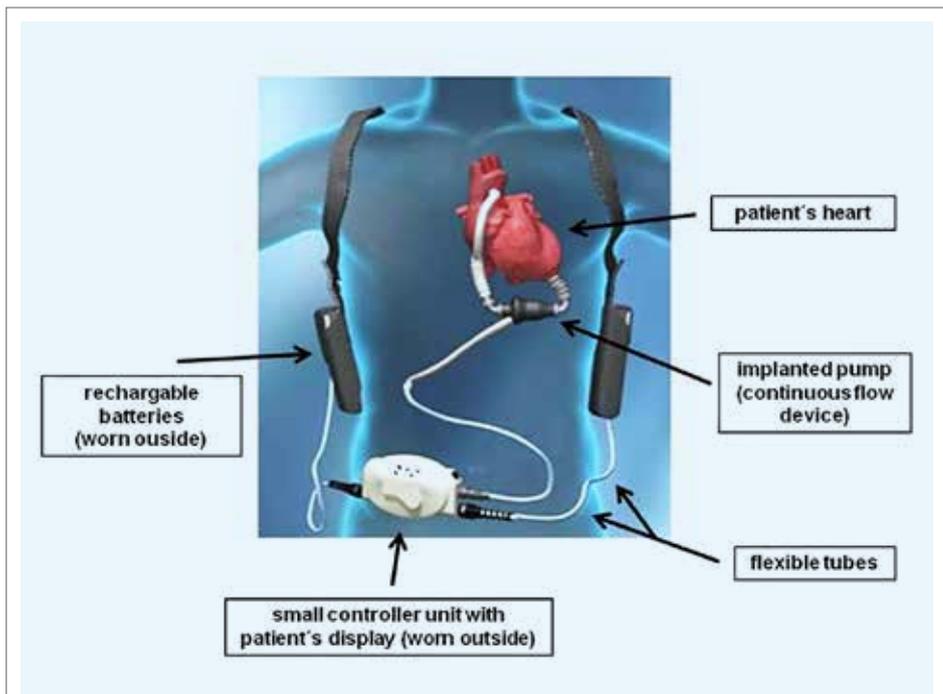


Figure 1

Components of the HeartMate II continuous-flow left ventricular assist device system, including pump, driveline, system controller, and batteries.; www.thoratec.com: with courtesy from Thoratec

oxygen saturation of 97% while he was breathing ambient air. The Heart sounds were faint with a regular rhythm and audible evidence of the continuous flow device. Resting 12-lead electrocardiogram showed sinus rhythm with 60 beats per minute. Echocardiography revealed a native left ventricular ejection fraction of 15%.

Exercise testing: An incremental exercise test was performed on an electrically braked cycle ergometer. Following warm up, the initial workload of 20 Watts (W) was increased by 10 W increments each minute until exhaustion. Heart rate was continuously monitored by a 12-lead electrocardiogram (ECC), blood pressure and clinical symptoms were assessed. The test was terminated due to dyspnea at 61 W.

Blood sampling: All samples of venous blood (20 ml; BD Vacutainer, Heidelberg, Germany) were drawn after a 10-hour overnight fast and at least 16 hours after training sessions. Routine laboratory blood analyses included HbA1c, fasting glucose and lipid profile (triglycerides, total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL); table 2).

Quality of life questionnaires: Psychological status and quality of life (QOL) were assessed by the MacNew heart disease health related questionnaire, which includes domains of emotional, physical, social and overall behavior (4,23). Possible scores range from 1 to 7, with a higher score indicating a better QOL.

Anxiety and Depression were assessed by the Hospital Anxiety and Depression Score (HADS) questionnaire (26). The HADS is a fourteen item scale that generates ordinal data. Seven of the items relate to anxiety and seven relate to depression. This questionnaire was applied to analyze the patient's behavior during the preceding two weeks.

Both the MacNew and HADS questionnaires have been shown to be valid, reliable and responsive instruments for measuring QOL of cardiac patients after myocardial infarction, heart failure and ischemic heart disease (5).

Questionnaires were handed out during the first and the last week of rehabilitation, and answers were reviewed and analyzed by a clinical psychologist.

Outpatient cardiac rehabilitation

Exercise training: The patient underwent a structured physical exercise training program for two hours once a week for nine months. Endurance exercise training was performed on an electrically-braked-cycle ergometer (Ergoline® ergoselect 100, Erlangen, Germany) and heart rate was measured continuously with a 3-lead-ECG. Blood pressure and oxygen saturation were assessed whenever a critical level of dyspnea or perceived exertion was reached. Each endurance training session was divided into 5 min of warm up, 40 min of training, and 5 min of cool down. Cycle ergometer training was performed at a target intensity of 60% of heart rate reserve (HRR; according to Karvonen et al.) (13).

During the first 4 weeks of cardiac rehabilitation his target training heart rate could not be reached, because of early-onset dyspnea and leg muscle fatigue. Thereafter, patient's fitness improved and his target heart rate could be reached.

Much to our surprise, after 3 and 5 months of training 2 episodes of accumulating pleural effusion occurred, requiring in-hospital treatment. After discharged his previous fitness was regained within 3 weeks.

In addition to cycle ergometer training 5 min of resistance exercise training was performed. Resistance training was initiated after 5 minutes of warm-up with stretching exercises. Then, various exercises for core stability were performed with an elastic training band (Theraband® green, Bisamberg, Austria) and included the 6 exercises for the upper body which the patient was expected to also complete at home at least on three days a week, for 15 repetitions each. Thereafter, 8 exercises for the upper and lower body were trained on weight lifting machines (Proxomed® compass, Alzenau, Germany). For each exercise the one repetition maximum (1RM) was determined, and training was performed with weights that permitted 10-12 repetitions and corresponded to 80% of 1RM (21). Weight was increased once the patient was able to perform more than 12 repetitions. All training sessions were supervised by a sports scientist or physiotherapist and a physician.

In addition, the patient was encouraged to perform resistance exercises at home according to an illustrated instructional manual which he received. It was his aim to meet minimum recommendations of 150 min of exercise training per week, as outlined in current national and international practice guidelines (7,21,25,29). Consistent with standardized practice for cardiac rehabilitation in Austria, the patient completed 4 units of dietary counseling but chose to only participate in 1 of 4 units of psychological group sessions.

Results

Anthropometrics, blood markers and exercise capacity are listed in table 2. As a result of nine months of exercise training, Pmax increased by 24%. Resting heart rate remained unchanged and a modest decline in both systolic and diastolic resting blood pressure of 10 and 5 mmHg respectively, were observed. Serum triglycerides, TC, HDL, LDL and HbA1c decreased during cardiac rehabilitation, whereas fasting blood glucose remained essentially unchanged. Body weight and body mass index increased modestly.

In keeping with current recommendations β -blocker and statin therapy was increased as tolerated. Furosemide could

Table 1

Overview of medication during outpatient cardiac rehabilitation at baseline and after 9 months.

| MEDICATION | OBSERVATION PERIOD | |
|-------------------------------------|--------------------|----------|
| | BASELINE | 9 MONTHS |
| Beta Blocker | | |
| Bisoprolol [mg] | 1,25 | 2,5 |
| Anti-Arrhythmica | | |
| Amiodaron [mg] | 200 | 200 |
| Anti-coagulant | | |
| Aspirin [mg] | 100 | 100 |
| Wafarin | INR | INR |
| Diuretica | | |
| Furosemide [mg] | 160 | 120 |
| Amiloride / Hydrochlorothiazid [mg] | 5/50 | 5/50 |
| Statins | | |
| Simvastatin [mg] | 20 | 40 |
| Others | | |
| Pantoprazol [mg] | 40 | 40 |
| Levothyroxin [μ g] | 25 | 50 |
| Allopurinol [mg] | 300 | 300 |
| Potassium [mg] | 3.9 | 4.7 |

Table 2

Measurements at baseline and after 9 months of cardiac rehabilitation; BMI=body mass index; RRsys=systolic blood pressure; RRdias=diastolic blood pressure; HRrest=resting heart rate; HRmax=maximum heart rate; Pmax=maximum power; HDL=high density lipoprotein; LDL=low density lipoprotein; HbA1c=glycated hemoglobin A1c.

| | RESULTS | |
|--------------------------|----------|----------|
| | BASELINE | 9 MONTHS |
| Anthropometrics | | |
| Weight [kg] | 97.5 | 101.0 |
| BMI [kg/m ²] | 30.3 | 31.5 |
| Exercise power | | |
| Pmax [Watt] | 61 | 76 |
| HRrest [beats/min] | 60 | 59 |
| RRsys [mmHg] | 100 | 90 |
| RRdias [mmHg] | 60 | 55 |
| Blood | | |
| Cholesterol [mg/dl] | 214 | 199 |
| HDL [mg/dl] | 100 | 91 |
| LDL [mg/dl] | 101 | 91 |
| Triglycerides [mg/dl] | 65 | 86 |
| Glucose [mg/dl] | 87 | 89 |
| HbA1c [%] | 6.1 | 5.2 |

be reduced, and potassium supplementation had to be slight increased.

Analysis of responses to the MacNew questionnaire revealed that physical, social and overall quality domains remained almost unchanged, whereas scores for emotional quality decreased. The HADS questionnaire revealed marginally increased T-values both at baseline and after 9 months (table 3).

Discussion

In this case report, one supervised two-hour training session each week augmented by voluntary, unsupervised home exercise training resulted in an improvement in Pmax after 9 months of rehabilitation. This is consistent with previous reports in patients with (15) mechanical assist devices, as well

as in patients with chronic heart failure (16,17). Importantly, this patient was able to achieve this improvement with just one supervised training session per week, suggesting that compliant patients with VADs may not require long-term intensive supervision and thus decreased resource allocation. The increase in Pmax of 24% is consistent with improvements previously documented in patients with chronic heart failure (19,20). Given his diminished left ventricular ejection fraction of 15%, improvement is likely attributable to both improved cardiac output and systemic circulation leading to peripheral muscle adaptation (1). No technical adjustments on the LVED system were performed during outpatient rehabilitation. Importantly, while exercise training led to an increase in Pmax, it likewise prevented the decline in physical function experienced by others awaiting cardiac transplantation, thus improving post-operative outcomes.

Ten months after finishing the outpatient rehabilitation our patient underwent heart transplantation. He successfully completed a prolonged in-hospital cardiac rehabilitation and is currently doing well.

There was a slight reduction in total cholesterol and LDL, most likely the result of intensified statin therapy, supported by exercise training. Further normalization of HbA1c might have been the result of endurance but also resistance training. The slight increase of body weight and body mass index is attributed to day-to-day changes in the extent of fluid retention despite optimal medical therapy.

The HADS questionnaire revealed a modest increase in anxiety and depression. Similarly, the MacNew questionnaire revealed unchanged values for the domains of physical, social and overall quality of life, but showed a decline in emotional quality at 9 months. In concurrence with our results, we know from other investigators that anxiety frequently coexists with depression and often exhibits a parallel increase in HADS scores (3) in people with heart disease. It is speculated that his decision to not participate in psychological sessions combined with the length of time on the device and mounting issues with respect to his socioeconomic worries may have contributed to these findings. Also, his disease-related early retirement poses economical strain on him and his family. Likewise, his medical status that included multiple hospitalizations combined with the long waiting period for an available organ may have contributed. These findings are consistent with recent work of Johannes et al. (29), who showed that not all patients benefited in all outcome measures in QOL to the same extent, and patients with higher levels of depression had poorer QOL outcomes. On the other hand, it may be speculated that his participation in cardiac rehabilitation might also have lessened the overall potential decline in psychosocial status that is frequently observed in patients with prolonged serious illness. As reported by others, poor QOL corresponds with the severity of advanced and end-stage heart failure (6,8,18), so interventions that modify any deterioration in QOL, particularly given the clinical status of this patient, are important.

Sullivan et al. (27) additionally described 3 core symptoms, fatigue, chest pain and breathlessness, for chronic heart failure, which also were found in our patient. They were strongly associated with anxiety and have been shown to be related to depression. The more severe the symptom(s), the more likely the patient was to be depressed. Indeed, during both episodes of progressive pleural effusion our patient complained of all 3 symptoms mentioned above in a very strong manner, which may coincide with our findings and may also be related to the low baseline values and the low decline in HADS-A and HADS-D,

Table 3

Quality of life—Outcomes of HADS questionnaire at baseline and after 9 months of cardiac rehabilitation; HADS=Hospital Anxiety and Depression Scale.

| HADS—ANXIETY QUESTIONNAIRE (ADJUSTED IN SEX AND AGE) | | | |
|---|-----------|---------|---------|
| time | raw value | range % | T-value |
| baseline | 11 | 85.6 | 60.6 |
| 9 months | 12 | 90.7 | 63.2 |
| HADS—DEPRESSION QUESTIONNAIRE (ADJUSTED IN SEX AND AGE) | | | |
| time | raw value | range % | T-value |
| baseline | 9 | 85.8 | 60.7 |
| 9 months | 11 | 93.0 | 64.8 |

respectively. In addition, the patient's anxiety relative to ICD firing, the risk of infection and the awareness of the long time period for the awaited HTX (over two years) also may have been contributing factors, as described by Grady et al. (9).

Conclusion

The purpose of this case report was to describe the effects of 9 months outpatient cardiac rehabilitation on exercise capacity and quality of life (QOL) in a patient with a left ventricular assist device. What is unique about this patient is the complex clinical status and his responses to just one supervised training session per week, which was supplemented by home-based exercise training, suggesting that compliant patients with LVADs may not require continuous supervision and thus decreased resource allocation. Furthermore, in our case we can confirm that combined endurance and resistance exercise training can be safely provided to a patient utilizing ventricular assist technology. However, since it cannot be excluded that the two episodes of pulmonary and peripheral edema where at least partially triggered by exercise training, patient awareness, daily weighing and regular patient assessment have to be part of an exercise intervention also in these patients.

There was an improvement in Pmax and only a subtle decline in his psychosocial status, which may have been worse without outpatient cardiac rehabilitation as observed in other very ill patients.

In summary, in this case, the outpatient cardiac rehabilitation program was a safe and effective therapy helping to achieve the patient's goals of improved Pmax and QOL.

Acknowledgements

The authors wish to thank all members of our outpatient cardiac rehabilitation team for their assistance in managing this patient during his course of therapy and providing their expertise for this manuscript. ■

Conflict of interest

The authors have no conflict of interest

References

- (1) ADAMS V, NIEBAUER J. Reversing Heart Failure-Associated Pathophysiology with Exercise: What Actually Improves and by How Much? *Heart Fail Clin*. 2015;11:17-28. doi:10.1016/j.hfc.2014.08.001
- (2) ARENA R, HUMPHREY R, MCCALL R. Altered exercise pulmonary function after left ventricular assist device implantation. *J Cardiopulm Rehabil*. 1999;19:344-346. doi:10.1097/00008483-199911000-00003
- (3) CARNEY RM, FREEDLAND KE, SHELIN YI, WEISS ES. Depression and coronary heart disease: a review for cardiologists. *Clin Cardiol*. 1997;20:196-200. doi:10.1002/clc.4960200304
- (4) DIXON T, LIM LL, OLDRIDGE NB. The MacNew heart disease health-related quality of life instrument: reference data for users. *Qual Life Res*. 2002;11:173-183. doi:10.1023/A:1015005109731
- (5) DIXON T, LIM LL, POWELL H, FISHER JD. Psychosocial experiences of cardiac patients in early recovery: a community-based study. *J Adv Nurs*. 2000;31:1368-1375. doi:10.1046/j.1365-2648.2000.01406.x
- (6) DRACUP K, WALDEN JA, STEVENSON LW, BRECHT ML. Quality of life in patients with advanced heart failure. *J Heart Lung Transplant*. 1992;11:273-279.
- (7) GARBER CE, BLISSMER B, DESCHENES MR, FRANKLIN BA, LAMONTE MJ, LEE IM, NIEMAN DC, SWAIN DP. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*. 2011;43:1334-1359. doi:10.1249/MSS.0b013e318213fefb
- (8) GRADY KL, JALOWIEC A, WHITE-WILLIAMS C, PIFARRE R, KIRKLIN JK, BOURGE RC, COSTANZO MR. Predictors of quality of life in patients with advanced heart failure awaiting transplantation. *J Heart Lung Transplant*. 1995;14:2-10.
- (9) GRADY KL, WARNER STEVENSON L, PAGANI FD, TEUTEBERG J, PAMBOUKIAN SV, BIRKS E, MOORE S, KIRKLIN JK. Beyond survival: recommendations from INTERMACS for assessing function and quality of life with mechanical circulatory support. *J Heart Lung Transplant*. 2012;31:1158-1164. doi:10.1016/j.healun.2012.08.020
- (10) HELMAN DN, ROSE EA. History of mechanical circulatory support. *Prog Cardiovasc Dis*. 2000;43:1-4. doi:10.1053/pcad.2000.7194
- (11) HERAN BS, CHEN JMH, EBRAHIM S, MOXHAM T, OLDRIDGE N, REES K, THOMPSON DR, TAYLOR RS. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev*. 2011. doi:10.1002/14651858.CD001800.pub2
- (12) HUMPHREY R. Exercise physiology in patients with left ventricular assist devices. *J Cardiopulm Rehabil*. 1997;17:73-75. doi:10.1097/00008483-199703000-00001
- (13) KARVONEN MJ, KENTALA E, MUSTALA O. The effects of training on heart rate: a longitudinal study. *Ann Med Exp Biol Fenn*. 1957;35:307-315.
- (14) KENNEDY MD, HAYKOWSKY M, HUMPHREY R. Function, eligibility, outcomes, and exercise capacity associated with left ventricular assist devices: exercise rehabilitation and training for patients with ventricular assist devices. *J Cardiopulm Rehabil*. 2003;23:208-217. doi:10.1097/00008483-200305000-00009
- (15) LAOUTARIS ID, DRITSAS A, ADAMOPOULOS S, MANGINAS A, GOUZIOUTA A, KALLISTRATOS MS, KOULOPOULOU M, VOUDRIS V, COKKINOS DV, SFIRAKIS P. Benefits of physical training on exercise capacity, inspiratory muscle function, and quality of life in patients with ventricular assist devices long-term postimplantation. *Eur J Cardiovasc Prev Rehabil*. 2011;18:33-40.
- (16) MEYER K, GORNANDT L, SCHWAIBOLD M, WESTBROOK S, HAJRIC R, PETERS K, BENEKE R, SCHNELLBACHER K, ROSKAMM H. Predictors of response to exercise training in severe chronic congestive heart failure. *Am J Cardiol*. 1997;80:56-60. doi:10.1016/S0002-9149(97)00283-X
- (17) MEYER K, SAMEK L, SCHWAIBOLD M, WESTBROOK S, HAJRIC R, BENEKE R, LEHMANN M, ROSKAMM H. Interval training in patients with severe chronic heart failure: analysis and recommendations for exercise procedures. *Med Sci Sports Exerc*. 1997;29:306-312. doi:10.1097/00005768-199703000-00004
- (18) NASSER EH, OVERHOLSER JC. Recovery from major depression: the role of support from family, friends, and spiritual beliefs. *Acta Psychiatr Scand*. 2005;111:125-132. doi:10.1111/j.1600-0447.2004.00423.x
- (19) NIEBAUER J, CLARK AL, WEBB-PEPLOE KM, BOGER R, COATS AJ. Home-based exercise training modulates pro-oxidant substrates in patients with chronic heart failure. *Eur J Heart Fail*. 2005;7:183-188. doi:10.1016/j.ejheart.2004.06.001
- (20) NIEBAUER J, CLARK AL, WEBB-PEPLOE KM, COATS AJ. Exercise training in chronic heart failure: effects on pro-inflammatory markers. *Eur J Heart Fail*. 2005;7:189-193. doi:10.1016/j.ejheart.2004.07.012
- (21) NIEBAUER J, MAYR K, TSCHENTSCHER M, POKAN R, BENZER W. Outpatient cardiac rehabilitation: the Austrian model. *Eur J Prev Cardiol*. 2013;20:468-479. doi:10.1177/2047487312446137
- (22) O'CONNOR CM, WHELLAN DJ, LEE KL, KETEYIAN SJ, COOPER LS, ELLIS SJ, LEIFER ES, KRAUS WE, KITZMAN DW, BLUMENTHAL JA, RENDALL DS, MILLER NH, FLEG JL, SCHULMAN KA, MCKELVIE RS, ZANNAD F, PINA IL. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA*. 2009;301:1439-1450. doi:10.1001/jama.2009.454
- (23) OLDRIDGE N, GUYATT G, JONES N, CROWE J, SINGER J, FEENY D, MCKELVIE R, RUNIONS J, STREINER D, TORRANCE G. Effects on quality of life with comprehensive rehabilitation after acute myocardial infarction. *Am J Cardiol*. 1991;67:1084-1089. doi:10.1016/0002-9149(91)90870-Q
- (24) PERK J, DE BACKER G, GOHLKE H, GRAHAM I, REINER Z, VERSCHUREN M, ALBUS C, BENLIAN P, BOYSEN G, CIFKOVA R, DEATON C, EBRAHIM S, FISHER M, GERMANO G, HOBBS R, HOES A, KARADENIZ S, MEZZANI A, PRESCOTT E, RYDEN L, SCHERER M, SYVANNE M, SCHOLTE OP REIMER WJ, VRINTS C, WOOD D, ZAMORANO JL, ZANNAD F. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). *Eur Heart J*. 2012;33:1635-1701. doi:10.1093/eurheartj/ehs092
- (25) PIEPOLI MF, CORRA U, BENZER W, BJARNASON-WEHRENS B, DENDALE P, GAITA D, MCGEE H, MENDES M, NIEBAUER J, ZWISLER ADO, SCHMID JP. Secondary prevention through cardiac rehabilitation: from knowledge to implementation. A position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev R*. 2010;17:1-17. doi:10.1097/HJR.0b013e3283313592
- (26) SNAITH RP. The Hospital Anxiety And Depression Scale. *Health Qual Life Outcomes*. 2003;1:29. doi:10.1186/1477-7525-1-29
- (27) SULLIVAN M, LEVY WC, RUSSO JE, SPERTUS JA. Depression and health status in patients with advanced heart failure: a prospective study in tertiary care. *J Card Fail*. 2004;10:390-396. doi:10.1016/j.cardfail.2004.01.011
- (28) TAKANO H, NAKATANI T, TAENAKA Y, KITHO Y, HIRAMORI K, HAZE K, ITOH A, FUJITA T, MANABE H. Treatment of Acute Profound Heart-Failure by Ventricular Assist Device. *Jpn Circ J*. 1992;56:100-110. doi:10.1253/jej.56.100
- (29) YOHANNES AM, DOHERTY P, BUNDY C, YALFANI A. The long-term benefits of cardiac rehabilitation on depression, anxiety, physical activity and quality of life. *J Clin Nurs*. 2010;19:2806-2813. doi:10.1111/j.1365-2702.2010.03313.x