Humanwissenschaftliche Fakultät

Rona Reibis | Annett Salzwedel | Hermann Buhlert | Karl Wegscheider | Sarah Eichler | Heinz Völler

Impact of training methods and patient characteristics on exercise capacity in patients in cardiovascular rehabilitation

Suggested citation referring to the original publication:
European Journal of Preventive Cardiology 23 (2016) 5, pp. 452–456
DOI http://dx.doi.org/10.1177/2047487315600815
ISSN (print) 2047-4873
ISSN (online) 2047-4881

European Journal of
Preventive
Cardiology

EUROPEAN SOCIETY OF CARDIOLOGY®

Original scientific paper

European Journal of Preventive Cardiology
2016, Vol. 23(5) 452–459

DOI: 10.1177/2047487315600815
ejpc.sagepub.com
SAGE

Impact of training methods and patient characteristics on exercise capacity in patients in cardiovascular rehabilitation

Rona Reibis[1], Annett Salzwedel[2], Hermann Buhlert[3], Karl Wegscheider[4], Sarah Eichler[2] and Heinz Völler[2,3]

Abstract

Aim: We aimed to identify patient characteristics and comorbidities that correlate with the initial exercise capacity of cardiac rehabilitation (CR) patients and to study the significance of patient characteristics, comorbidities and training methods for training achievements and final fitness of CR patients.

Methods: We studied 557 consecutive patients (51.7 ± 6.9 years; 87.9% men) admitted to a three-week in-patient CR. Cardiopulmonary exercise testing (CPX) was performed at discharge. Exercise capacity (watts) at entry, gain in training volume and final physical fitness (assessed by peak O_2 utilization (VO_{2peak}) were analysed using analysis of covariance (ANCOVA) models.

Results: Mean training intensity was 90.7 ± 9.7% of maximum heart rate (81% continuous/19% interval training, 64% additional strength training). A total of 12.2 ± 2.6 bicycle exercise training sessions were performed. Increase of training volume by an average of more than 100% was achieved (difference end/beginning of CR: 784 ± 623 watts $\times$ min). In the multivariate model the gain in training volume was significantly associated with smoking, age and exercise capacity at entry of CR. The physical fitness level achieved at discharge from CR as assessed by VO_{2peak} was mainly dependent on age, but also on various factors related to training, namely exercise capacity at entry, increase of training volume and training method.

Conclusion: CR patients were trained in line with current guidelines with moderate-to-high intensity and reached a considerable increase of their training volume. The physical fitness level achieved at discharge from CR depended on various factors associated with training, which supports the recommendation that CR should be offered to all cardiac patients.

Keywords

Cardiac rehabilitation, exercise tests, cardiorespiratory fitness, multivariate modelling

Received 25 May 2015; accepted 24 July 2015

Background

Subsequent to an acute coronary event (ACS), or cardiac intervention, patients require special attention to maintain or improve their functional capacity, or to restore their quality of life, respectively.[1] Such cardiac rehabilitation (CR) is frequently performed in form of structured, multifaceted and interdisciplinary programmes. While the programmes differ in many details, the objectives and core components are well established.[2–4] The latter include baseline patient assessment, nutritional counselling, risk factor management (lipids, blood pressure, weight, diabetes mellitus and smoking), psychosocial interventions, nutritional and physical activity counselling as well as exercise training.[5] In patients after a cardiovascular event, physical activity needs to be tailored to the individual's exercise capacity

[1]Cardiological Outpatient Clinic, Am Park Sanssouci, Potsdam, Germany
[2]Center of Rehabilitation Research, University of Potsdam, Germany
[3]Department of Cardiology, Klinik am See, Rüdersdorf, Germany
[4]Department of Medical Biometry and Epidemiology, University Medical Center, Hamburg-Eppendorf, Germany

Corresponding author:
Heinz Völler, Center of Rehabilitation Research, University of Potsdam, Am Neuen Palais 10, Haus 12 D-14469 Potsdam, Germany
Email: heinz.voeller@uni-potsdam.de

and risk profile, with the aim to reach and maintain each individual's highest possible fitness level and to safely perform endurance exercise training 30–60 min daily (3–5 days per week) in combination with resistance training 2–3 times a week. Sufficiently high training intensities should be sought.[5]

A number of systematic reviews, including Cochrane reviews, have clearly demonstrated significant benefits in clinical outcomes (reduced all-cause and cardiac mortality, nonfatal re-infarction and reduced hospitalization rates) and changes in modifiable risk factors (total cholesterol, triglycerides and systolic blood pressure), respectively in patients after CR.[6,7] Therefore, CR programmes are strongly recommended (Class I indication) for patients after a cardiovascular event by the European Society of Cardiology, the American Heart Association, the American College of Cardiology and other professional societies.[8–11]

Against this background, we analysed data from the patient database of our CR unit to address the questions, (a) whether training is performed according to the current guidelines, (b) what determines the exercise capacity at the initiation of CR, (c) does the physical fitness, measured by VO_{2peak} at discharge from CR, depend on patient characteristics and training effects.

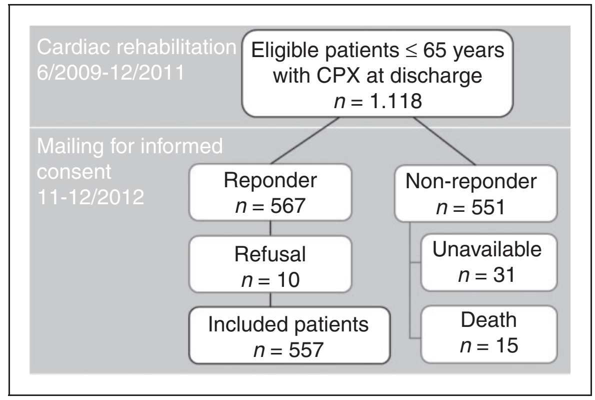

Figure 1. Flow chart of inclusion process. CPX: cardiopulmonary exercise testing.

Methods

The present study was a retrospective analysis of patient data in the electronic patient files of the Klinik am See, a rehabilitation centre for cardiovascular diseases. Patients, as a rule, are transferred for a standardized multicomponent three-week in-patient CR programme after treatment for a cardiovascular event from an acute hospital. CR includes patient education, diet counselling, psychological support, risk factor management as well as training components (bicycle exercising, (Nordic) walking, strength training).

Between June 2009–December 2011, 1118 patients younger than 65 years and occupied (employed or self-employed) attended the CR programme and underwent cardiopulmonary exercise (CPX) testing before discharge. For the present analysis, all patients were contacted by mail. Finally, 557 patients gave their informed consent and were included into the analysis (Figure 1).

At admission to CR, patients underwent a symptom-limited bicycle exercise stress test to determine exercise intensity. Training volume as a product of exercise intensity (watts) and exercise time (min) was collected at entry and end of CR.

Cardiopulmonary exercise testing with respiratory gas analysis was performed using the modified Naughton treadmill protocol.[12] Peak O_2 utilization (VO_{2peak}) was defined as the highest VO_2 value in ml/kg/min (or max O_2 utilization with an oxygen uptake steady-state plateau averaged over 20–30 s), achieved at individual maximum load during incremental exercise testing. The VE/VCO_2 slope specifies the relationship between minute ventilation (VE) and carbon dioxide output (VCO_2), and represents a global parameter of respiratory efficiency. A satisfactory cardiopulmonary exercise test was characterized by a respiratory exchange ratio $(RER) > 1.1$, which indicates complete metabolic exertion. During rest, during exercise, and after exercise, regular blood pressure measurements and single-breath manoeuvres were scheduled to generate intra-breath curves. The standard values of Wasserman et al. were used.[13] Blood lactate levels were not assessed routinely.

The variables extracted from the database comprised socio-demographic and clinical parameters, lipid profile, comorbidities including parameters of cardiac function (from exercise testing, or two-dimensional echocardiography to assess systolic and diastolic dysfunction as well as left ventricular mass), and training volume at admission and at discharge (watts × time unit).

Patients' occupations were characterized as light (<4 metabolic equivalents (METs, $1\ MET = 3.6\ ml \times kg^{-1} \times min^{-1}$)), light to moderate (<6 METs), moderate (<8 METs) and heavy profile (>8 METs).

The study protocol was approved by the ethics committee of the University of Potsdam. Data protection rules were closely observed, and patient data were processed anonymously.

Statistics

To demonstrate small effect sizes of 0.25 standard deviations (SDs), around 500 evaluable patients are required. We calculated that the collection of data from three years would be sufficient to reach the required number of patients.

Descriptive analysis was performed as absolute and relative frequencies for categorical variables and as mean ± SD for continuous variables. To determine the factors with dominant impact on (a) the initial exercise capacity (watts) at bicycle exercise stress test of the patients, (b) the percentage gain in training volume and (c) the final fitness of the patients (VO_{2peak}), regression models were fitted to the data. First, the training volume tolerated at the first exercise test was regressed to all patient characteristics determined at admission. Subsequently the percentage gain in training volume was studied with the same covariates in an analysis of covariance (ANCOVA)-like regression analysis where the baseline training volume was additionally included in the model. We preferred to use the percentage gain as compared to the absolute gain since the model fit was better and the residual distribution of the percentage model was nearly normal. Finally, we regressed the final fitness as measured by VO_{2peak} (a) to the patient characteristics alone, (b) to patient characteristics, training volume and training methods together in order to find out which percentages the final fitness depends on: the initial exercise capacity or the training successes. For this purpose we report r^2 values of the two models and the partial eta squared of the most relevant factors or covariates as measures of the variance explained by models or uniquely by certain factors.

Results

A total of 557 patients were eligible for analysis. Patient characteristics, risk factors and comorbidities are displayed in Table 1. Overall, patients were 52 ± 7 years old, with substantially more men (88%) than women (12%). The last reported work was light in 25.1%, light-to-moderate in 30.3%, moderate in 38.1%, and heavy in 6.5%.

Index diseases that rendered patients eligible for CR were mostly percutaneous coronary intervention (PCI) with or without ACS (62%), followed by coronary artery bypass grafting, valve surgery or other interventions or diseases.

Training parameters

Echocardiographic and electrocardiogram (ECG) findings at CR initiation are shown in Table 2. On ergometry, mean exercise capacity of patients was 115 ± 36 watts, and mean heart rate was 119 ± 19 beats per min. Left ventricular systolic function was reduced (left ventricular ejection fraction (LVEF) ≤ 40%) in 12.5%, and diastolic dysfunction was noted in 59.8% of the cohort.

Table 1. Patient characteristics at cardiac rehabilitation (CR) initiation.

Age, years	51.7 ± 6.9
Gender (male)	489 (87.9%)
NYHA I/II/III/IV	58.6%/33.6%/7.7%/0%
6-Min walk distance, m	395 ± 73
Indication for CR	
PCI with/without ACS	348 (62.5%)
CABG	90 (16.2%)
Valve surgery	53 (9.5%)
Other[a]	66 (11.8%)
Hospital stay (days)	9.6 ± 8
Risk factors	
Arterial hypertension	411 (73.8%)
Hyperlipoproteinaemia	382 (68.6%)
Current smoking	156 (28.0%)
Ex-smoking (≥5 years)	268 (48.1%)
Comorbidities, number	0.5 ± 0.7
Diabetes mellitus	100 (18.0%)
COPD	21 (3.8%)
Joint, spine pain	131 (23.5%)
Medication	
Beta blocker	495 (88.9%)
ACE inhibitor	401 (72.0%)
Angiotensin receptor blocker	78 (14.0%)
Aldosterone antagonist	65 (11.7%)

ACE: angiotensin converting enzyme; ACS: acute coronary syndrome; ARB: angiotensin receptor blocker; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; PCI: percutaneous coronary intervention. Values indicate *n* (%) or mean ± standard deviation.
[a]Other indications include pulmonary embolism, dilatative cardiomyopathy and myocarditis.

Factors associated with exercise capacity at initiation of CR

The forest plot in Figure 2 displays parameters that were associated with maximum capacity in bicycle exercise stress test at CR initiation. Factors significantly associated with higher exercise capacity (increase in watts) were PCI as main diagnosis (vs other diagnoses), light professional activities (vs heavy work), and preserved LVEF. On the contrary, factors significantly associated with lower exercise capacity were female gender, previous heart valve replacement, higher age and higher number of comorbidities. No significant association was found for light/moderate or moderate work as last activity and coronary artery bypass graft (CABG) as main diagnosis. The effect sizes were considerable and ranged from + 21.1 watts (presence of PCI diagnosis) to −40.4 watts (female gender).

Endurance training was reported in all patients. An average number of 12.2 ± 2.6 training sessions were performed. Mostly based on their systolic function, patients performed continuous training more often than interval training (80.9% versus 19.1%). A heart rate of 107 ± 14 beats per minute was reported, which corresponds to $90.7 \pm 9.7\%$ of the maximum rate achieved. In categorical terms, $\leq 85\%$ of maximum heart rate were noted in 21%, $\leq 75\%$ of maximum in 3.2%. Training volume increased by an average of more than 100% (difference end/beginning of CR: 784 ± 623 watts $\times$ min). Additionally, all patients had walking sessions (8.3 ± 3.3). Strength training was administered to 63.6% of patients with 6.4 ± 4.5 sessions during CR.

Table 2. Echocardiographic and electrocardiogram (ECG) findings at cardiac rehabilitation (CR) initiation.

Parameter	Value
2-D-Echo	
Systolic function	
Left ventricular ejection fraction (%)	54.5 ± 9.2
$\leq 40\%$	57 (12.5%)
Diastolic function	
Normal	188 (40.2%)
Diastolic dysfunction I°	154 (32.9%)
Diastolic dysfunction II°	104 (22.2%)
Diastolic dysfunction III°	22 (4.7%)
LVM (g/H)$^{2.7}$	53.9 ± 14.9
ECG	
Sinus rhythm	411 (97.2%)
Atrial fibrillation	12 (2.8%)
Exercise ECG at admission	
Maximum exercise capacity (watts)	115 ± 36
Max heart rate (min^{-1})	119 ± 19

LVM: left ventricular mass. Values indicate *n* (%) or mean ± standard deviation.

Change of training volume during CR

The only factor which was statistically significantly associated with an increase of training volume (watts $\times$ min; Figure 3) was increased exercise capacity at CR entry; a non-significant trend for increased volume was noted for PCI and light work. Factors significantly associated with decreased training volume were current smoking, number of comorbidities and age.

Physical fitness at discharge

Only $r^2 = 29.4\%$ of the observed variation in final fitness as determined by VO_{2peak} at discharge from CR could be attributed to patient-related factors. If training factors were added to the model, the explained variance increased to $r^2 = 43.0\%$. Table 3 shows the contributions of factors and covariates. Of the patient-related factors, age (7.7% of total effect), indication for CR and gender

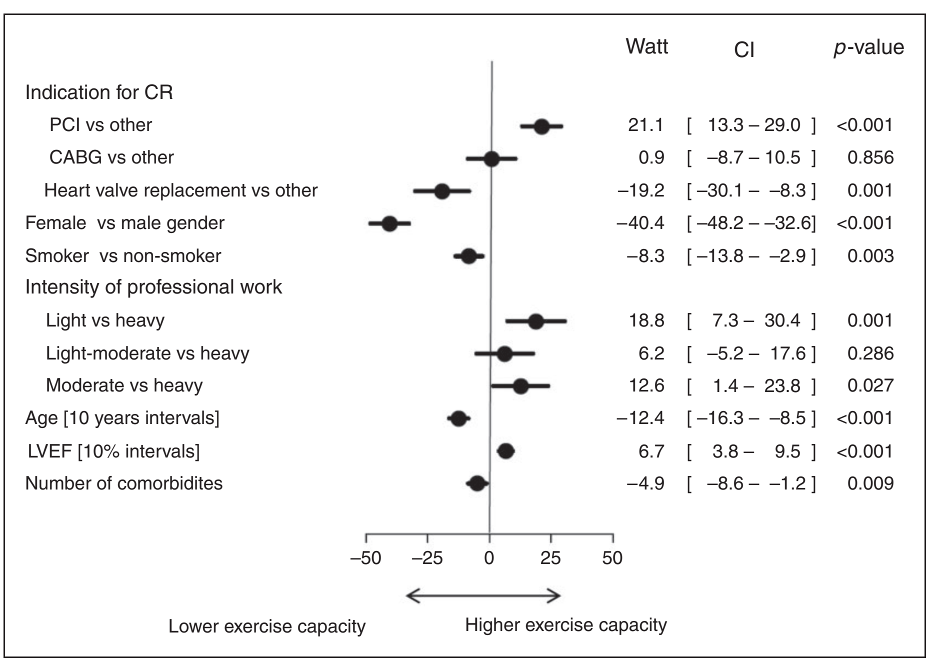

Figure 2. Impact of patient characteristics on exercise capacity (bicycle stress test) at initiation of cardiac rehabilitation (CR). The forest plot displays mean effect (bullet) and 95% confidence intervals (CIs, horizontal lines). The vertical line (0) represents 'no effect', while bullets right to the line represent increased training volume, left to the line decreased training volume. CABG: coronary artery bypass graft; LVEF: left ventricular ejection fraction (%); PCI: percutaneous coronary intervention.

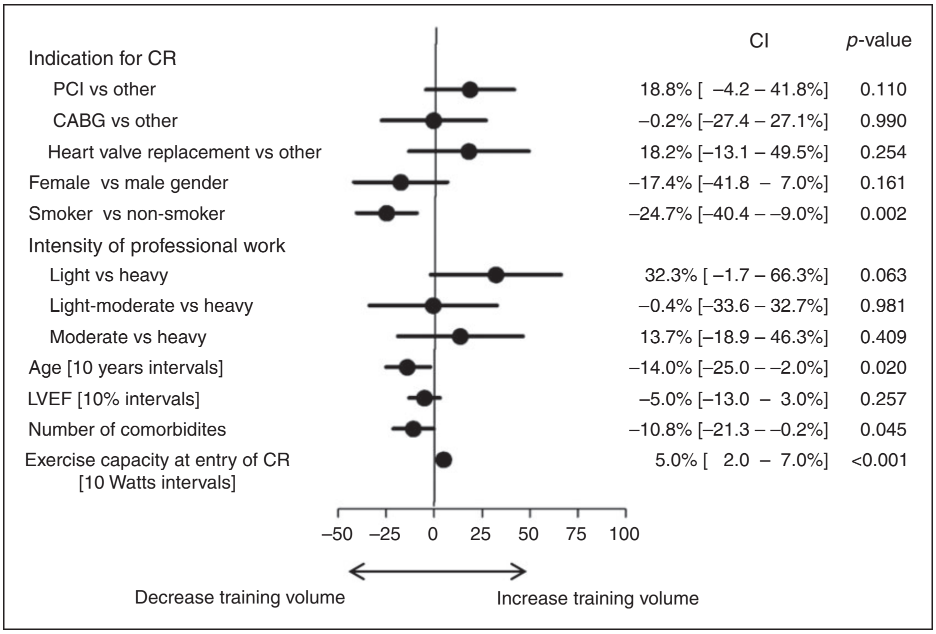

Figure 3. Impact of patient characteristics on gain in training volume (%) during the cardiac rehabilitation (CR) stay. The forest plot displays mean effect (bullet) and 95% confidence intervals (CIs, horizontal lines). The vertical line (0) represents 'no effect', while bullets right to the line represent increased training volume, left to the line decreased training volume. CABG: coronary artery bypass graft; LVEF: left ventricular ejection fraction (%); PCI: percutaneous coronary intervention.

Table 3. Determinants of physical fitness (peak O_2 utilization (VO_{2peak})) at discharge from cardiac rehabilitation (CR).

Variable	*p* Value	Partial eta squared (explained variance) %
Demography and patient characteristics		
Age, years	<0.001	7.7
Gender, female/male	0.033	1.0
Blue/white collar work	0.183	1.1
Comorbidities, risk factors and cardiac function		
Number of comorbidities	0.305	0.2
Smoking	0.441	0.1
Left ventricular ejection fraction, %	0.505	0.1
Indication for cardiac rehabilitation[a]	0.024	2.1
Training factors		
Exercise capacity at entry of CR, watts max	<0.001	3.6
Training intensity, % of heart rate	0.975	0.0
Increase of training volume, watts × min	<0.001	4.2
Additional strength training, yes/no	0.824	0.0
Training method, continuous/interval	<0.001	3.0

The table shows which percentages the final fitness (VO_{2peak}) depend on the most important variables. For example, the variables 'exercise capacity at entry of CR' and 'increase of training volume' explain the fitness together to the same amount as the variable 'age'.
[a]Percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), heart valve replacement/other.

uniquely explained significant percentages of the variance between patients. Of the training factors, increase of training volume, maximum exercise capacity at initiation of CR and training method contributed significantly to the explained variance. Of note, no additional contributions were found for LVEF, number of comorbidities, smoking, training intensity and additional strength training.

Discussion

According to this analysis, during a three-week structured CR, patients underwent mainly endurance training and in part additional strength training with high intensity, in line with current guideline recommendations. They achieved a doubling of training volume within a short time frame.

Fitness at the end of CR as determined by VO_{2peak} was mainly influenced by age, the exercise capacity at initiation of CR and increase of training volume, respectively.

The role of graded (incremental) exercise testing in order to directly evaluate functional capacity to patients entering CR is part of guideline recommendations of various societies.[14–16] In our institution, too, the bicycle exercise stress test is a standard tool for initial patient assessment including risk stratification and individualized exercise prescription.[17]

Measured peak aerobic capacity (VO_{2peak}) is the most accurate objective and reproducible parameter of exercise capacity (usually by symptom-limited treadmill testing), which in turn is a powerful independent predictor of prognosis in men and women with known or suspected coronary disease referred for CR.[18,19] Cardiopulmonary exercise testing is generally a safe procedure, even in a population with underlying high-risk cardiovascular diagnoses.[20]

VO_{2peak} values on entry to CR have been reported to be extremely low, particularly in women, approaching values seen in patients with severe chronic heart failure. This underscores the importance of CR after a major cardiac event to improve physical function and long-term prognosis.[21]

Patients underwent aerobic endurance training with modalities being in line with current recommendations.[5] Aerobic training in the moderate-to-high-intensity domain is supported by strong evidence in patients with both preserved and reduced left ventricular function.[22–24] Continuous training, for which the majority of evidence in the literature is available,[2] was much more often applied than interval training in our study (81% vs 19%). Resistance strength training was frequently performed as well (63%), in line with other studies, confirming it is effective and also well tolerated in patients after a cardiovascular event.[25] Indeed, the risk of cardiovascular complications is not higher after high-intensity exercise compared to moderate-intensity exercise in a cardiovascular rehabilitation setting as shown in a recent study in Norway.[26]

In the analysis of factors that are associated with physical performance (at CR initiation), the strongest effects were noted for gender: women not surprisingly had a lower performance of −40 watts. It has been described in a US study that women in exercise-based CR do have a significantly lower exercise capacity at the beginning of the programme compared to men (woman VO_{2peak} 14.5 vs men 19.3 ml/kg/min).[21] Patients after valve surgery in our study had a lower performance too, but comparative data on fitness in this patient group are very limited.[5] Conversely, patients with higher LVEF at entry and those with PCI (a less invasive procedure compared to CABG) as well as light (versus heavy) intensity of professional work also had significantly higher performance compared to patients without these conditions.

The effect on training volume from CR within three weeks can be substantial as shown in this study. Patients after PCI (e.g. less stressful intervention without thoracotomy) and those with previously light professional work as well as those with higher exercise capacity and CR entry obtained higher training volume increases.

In the analysis of determinants of physical fitness (VO_{2peak}) at the end of CR, the influence of individual patient-related factors but also training characteristics was surprisingly small. Age had the strongest relative, albeit in absolute terms moderate, influence (7.7% of total effect), followed by increase of training volume, training method and maximum exercise tolerance at entry. However, while age is an unchangeable parameter the training variables can be influenced during CR. Interestingly, not only the index diagnosis, comorbidities, LVEF, gender, but also training intensity or additional strength training had no (or only negligible) impact on fitness. As only few patient-related factors (that in addition cannot be modified) influenced physical fitness, it can be concluded that it is CR per se which independently increases fitness.

Methodological considerations

Among the strengths of the study was the availability of rather complete datasets with respect to clinical characteristics and exercise test results. Otherwise, while the volume of endurance training is well documented, the individually prescribed additional training components such as strength training or walking are difficulty to quantify.

The study was monocentric, the clinic is associated with an established research centre and therefore the institution likely to adhere to the current guidelines. However, characteristics of patients in this study were similar to cohorts in other CR institutions in Germany.[27,28] The study cohort is at low risk, with mean age 51.7 years, because CPX was only performed as an objective assessment for evaluation of ability to work. Other limitations of our study are those inherent to any retrospective database analysis.[29] The time frame of observation is limited to the typical three-week

CR period which is covered by health insurance in Germany. Long-term assessments were not performed due to logistical reasons, but they are needed, as the positive physiological and clinical effects of training disappear after one month of detraining.[30,31]

Conclusion

Patients underwent training sessions with moderate-to-high intensity in accordance with guideline recommendations and reached a considerable increase of their training volume by the end of the CR stay. The physical fitness level achieved at discharge from CR is dependent on age, but to a higher extent on various factors related to training (exercise capacity at entry, increase of training volume and training method). Since that the latter factors can be influenced, CR should be offered to all cardiac patients.

Acknowledgments

The authors acknowledge the input of David Pittrow with respect to interpretation of the dataset. Stefan Kaminski (deceased 2014) was involved in data collection for the purpose of an MD thesis. The data in this article were presented at the Annual Session of the European Society of Cardiology in Barcelona, Spain, September 2, 2014.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study was funded by an instructed grant from the German pension insurance Berlin-Brandenburg.

References

1. Piepoli MF, Corra U, Benzer W, et al. 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 Rehabil* 2010; 17: 1–17.
2. Leon AS, Franklin BA, Costa F, et al. Cardiac rehabilitation and secondary prevention of coronary heart disease: An American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2005; 111: 369–376.
3. Balady GJ, Ades PA, Bittner VA, et al. Referral, enrollment, and delivery of cardiac rehabilitation/secondary prevention programs at clinical centers and beyond: A presidential advisory from the American Heart Association. *Circulation* 2011; 124: 2951–2960.
4. Balady GJ, Williams MA, Ades PA, et al. Core components of cardiac rehabilitation/secondary prevention programs: 2007 Update: A scientific statement from the American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee, the Council on Clinical Cardiology; the Councils on Cardiovascular Nursing, Epidemiology and Prevention, and Nutrition, Physical Activity, and Metabolism; and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2007; 115: 2675–2682.
5. Vanhees L, Rauch B, Piepoli M, et al. Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular disease (Part III). *Eur J Prev Cardiol* 2012; 19: 1333–1356.
6. Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2011: CD001800.
7. Oldridge N. Exercise-based cardiac rehabilitation in patients with coronary heart disease: Meta-analysis outcomes revisited. *Future Cardiol* 2012; 8: 729–751.
8. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction–executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004; 44: 671–719.
9. Jneid H, Anderson JL, Wright RS, et al. 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/Non-ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2012; 126: 875–910.
10. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 Guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2007; 50: e1–e157.
11. Steg P, James S, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012; 33: 2569–2619.
12. Balady GJ, Arena R, Sietsema K, et al. Clinician's guide to cardiopulmonary exercise testing in adults: A scientific statement from the American Heart Association. *Circulation* 2010; 122: 191–225.
13. Wasserman K, Hansen J, Sue D, et al.. Normal Values. In: Weinberg R (ed.) *Principles of exercise testing and interpretation*, 4th ed. Philadelphia: Lippincott Williams and Wilkins, 2005, pp.160–182.

14. Corra U, Piepoli MF, Carre F, et al. Secondary prevention through cardiac rehabilitation: Physical activity counselling and exercise training: Key components of the position paper from the Cardiac Rehabilitation Section of the European Association of Cardiovascular Prevention and Rehabilitation. *Eur Heart J* 2010; 31: 1967–1974.
15. Balady GJ, Ades PA, Comoss P, et al. Core components of cardiac rehabilitation/secondary prevention programs: A statement for healthcare professionals from the American Heart Association and the American Association of Cardiovascular and Pulmonary Rehabilitation Writing Group. *Circulation* 2000; 102: 1069–1073.
16. Guazzi M, Adams V, Conraads V, et al. EACPR/AHA joint scientific statement. Clinical recommendations for cardiopulmonary exercise testing data assessment in specific patient populations. *Eur Heart J* 2012; 33: 2917–2927.
17. Mezzani A, Hamm LF, Jones AM, et al. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: A joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. *Eur J Prev Cardiol* 2013; 20: 442–467.
18. Kavanagh T, Mertens DJ, Hamm LF, et al. Peak oxygen intake and cardiac mortality in women referred for cardiac rehabilitation. *J Am Coll Cardiol* 2003; 42: 2139–2143.
19. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med* 2002; 346: 793–801.
20. Skalski J, Allison TG and Miller TD. The safety of cardiopulmonary exercise testing in a population with high-risk cardiovascular diseases. *Circulation* 2012; 126: 2465–2472.
21. Ades PA, Savage PD, Brawner CA, et al. Aerobic capacity in patients entering cardiac rehabilitation. *Circulation* 2006; 113: 2706–2712.
22. Adachi H, Koike A, Obayashi T, et al. Does appropriate endurance exercise training improve cardiac function in patients with prior myocardial infarction? *Eur Heart J* 1996; 17: 1511–1521.
23. Dubach P, Myers J, Dziekan G, et al. Effect of high intensity exercise training on central hemodynamic responses to exercise in men with reduced left ventricular function. *J Am Coll Cardiol* 1997; 29: 1591–1598.
24. Van Craenenbroeck EM, Hoymans VY, Beckers PJ, et al. Exercise training improves function of circulating angiogenic cells in patients with chronic heart failure. *Basic Res Cardiol* 2010; 105: 665–676.
25. Pollock ML, Franklin BA, Balady GJ, et al. AHA Science Advisory. Resistance exercise in individuals with and without cardiovascular disease: Benefits, rationale, safety, and prescription: An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association; Position paper endorsed by the American College of Sports Medicine. *Circulation* 2000; 101: 828–833.
26. Rognmo O, Moholdt T, Bakken H, et al. Cardiovascular risk of high- versus moderate-intensity aerobic exercise in coronary heart disease patients. *Circulation* 2012; 126: 1436–1440.
27. Rauch B, Riemer T, Schwaab B, et al. Short-term comprehensive cardiac rehabilitation after AMI is associated with reduced 1-year mortality: Results from the OMEGA study. *Eur J Prev Cardiol* 2014; 21: 1060–1069.
28. Schwaab B, Waldmann A, Katalinic A, et al. In-patient cardiac rehabilitation versus medical care – a prospective multicentre controlled 12 months follow-up in patients with coronary heart disease. *Eur J Cardiovasc Prev Rehabil* 2011; 18: 581–586.
29. Motheral B, Brooks J, Clark MA, et al. A checklist for retrospective database studies–report of the ISPOR Task Force on Retrospective Databases. *Value Health* 2003; 6: 90–97.
30. Volaklis KA, Douda HT, Kokkinos PF, et al. Physiological alterations to detraining following prolonged combined strength and aerobic training in cardiac patients. *Eur J Cardiovasc Prev Rehabil* 2006; 13: 375–380.
31. Vona M, Codeluppi GM, Iannino T, et al. Effects of different types of exercise training followed by detraining on endothelium-dependent dilation in patients with recent myocardial infarction. *Circulation* 2009; 119: 1601–1608.