Long-term effects of cardiac rehabilitation after heart valve surgery - results from the randomised CopenHeartVR trial

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Aims. The CopenHeartVR trial found positive effects of cardiac rehabilitation (CR) on physical capacity at 4 months. The long-term effects of CR following valve surgery remains unclear, especially regarding readmission and mortality. Using data from the CopenHeartVR trial we investigated long-term effects on physical capacity, mental and physical health and effect on mortality and readmission rates as specified in the original protocol. Methods. A total of 147 participants were included after heart valve surgery and randomly allocated 1:1 to 12-weeks exercise-based CR including a psycho-educational programme (intervention group) or control. Physical capacity was assessed as peak oxygen uptake (VO2 peak) measured by cardiopulmonary exercise testing, mental and physical health by Short Form-36 questionnaire, Hospital Anxiety and Depression Scale, and HeartQol. Mortality and readmission were obtained from hospital records and registers. Groups were compared using mixed regression model analysis and log rank test. Results. No differences in VO2 peak at 12 months or in self-assessed mental and physical health at 24 months (68% vs 75%, p = .120) was found. However, our data demonstrated reduction in readmissions in the intervention group at intermediate time points; after 3, 6 (43% vs 59%, p = .03), and 12 (53% vs 67%, p = .04) months, respectively, but no significant effect at 24 months. Conclusions. Exercise-based CR after heart valve surgery reduces combined readmissions and mortality up to 12 months despite lack of improvement in exercise capacity, physical and mental health long-term. Exercise-based CR can ensure short-term benefits in terms of physical capacity, and lower readmission within a year, but more research is needed to sustain these effects over a longer time period. These considerations should be included in the management of patients after heart valve surgery.

Introduction

The increasing number of patients with valve disease has led to a worldwide increase in heart valve procedures [1]. New complex treatment procedures and shorter length of hospital stay demands the management after valve surgery [2,3]. The heart valve clinic has been proposed for patients with valve disease [2–6]. However, less attention is paid to the period right after valve surgery in such clinics, and rehabilitation initiatives are not mentioned as part of the integrated approach. Usually patients have clinical follow up with echocardiography after valve surgery, and then, CR is offered in most centres but is not part of the integrated approach. Studies have shown high readmission rates after heart valve surgery at short term and long term [7–9], with readmission rates above 50% at 12 months after valve surgery [9]. These readmissions are often acute and caused by cardiac and non-cardiac causes [10]. An intensified follow-up
using an individualized approach has shown the potential to reduce readmissions after heart valve surgery [11].

Exercise-based cardiac rehabilitation (CR) is recommended after heart valve surgery and has shown positive short-term effects on physical capacity [13,14]. In various cardiac populations, exercise-based CR is also known to increase physical capacity and quality of life [9,12,15], but in patients following heart valve surgery, the evidence is unclear long term [13,14]. In patients with ischemic heart disease, CR has shown to reduce readmissions at 12 months [12]. Thus, exercise-based CR might reduce readmissions after heart valve surgery, but has never been investigated [13]. A Danish study found an association between physical activity and mortality among patients after heart valve surgery [16]. Though, the effects of exercise-based CR on mortality are not convincing [15]. Data investigating effects of follow-up after heart valve surgery on readmission and mortality is therefore crucial.

The randomised CopenHeartVR trial is the largest rehabilitation trial investigating the effect of CR after heart valve surgery and found a positive effect of CR on physical capacity but was neutral on mental health. Further data demonstrated cost savings at 6-month follow-up due to fewer in-patient hospital readmissions and less sick leave [10].

Through unique access to long-term follow-up data at 6, 12 and 24 months from the randomised CopenHeartVR trial, and linkage to Danish nationwide registers at the same time-points, it was possible to study long-term effects of exercise-based CR after heart valve surgery.

Thus, the aims of this study were; (1) to investigate the long-term effects of CR after heart valve surgery compared with the control group on physical capacity at 12 months and health-related quality of life at 12 and 24 months; (2) to investigate the composite effect of CR participation on overall readmissions, acute and elective readmissions and overall mortality and emergency room contacts at 3, 6, 12, 18 and 24 months.

In these exploratory analyses, we hypothesised that the effect of a 12 weeks exercise-based CR programme on physical capacity, health-related quality of life, mental health, and mortality and readmission will be similar to controls at long-term follow-up.

**Trial registration and ethical considerations**

The CopenHeartVR trial was approved by the local regional Research Ethics Committee (H-1-2011-157), and the Danish Data Protection Agency (j.nr. 2007-58-0015) and is registered at ClinicalTrials.gov (NCT01558765). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

**Methods**

**The CopenHeartVR trial**

We used data from the CopenHeartVR trial described elsewhere [14,17]. The trial investigated the effect of a CR programme after heart valve surgery including physical exercise and psychoeducation. This study is an explorative study based on secondary data collected as part of the pre-planned data collection [17].

**Population**

Inclusion criteria were patients ≥18 years of age with heart valve surgery irrespective of heart valve procedure and with no simultaneous ischemic heart disease, and informed written consent was obtained from each patient. Exclusion criteria were age below 18, pregnancy or participation in competition sports. Only patients undergoing heart valve surgery with sternotomy were included.

**Outcomes**

**Physical capacity**

Physical capacity was measured by peak oxygen uptake (VO2 peak) through cardiopulmonary exercise test with ventilatory gas analysis using a ramp protocol with initial workload of 25 or 50 watts, increasing by 12.5 watts/min gradually until exhaustion (protocol article). The test was performed at 1, 4 and 12 months after surgery.

Physical capacity was evaluated using 6 min Walk test and Sit to stand test, with number of repeated sits to stand from chair within 15 s.

**Health related quality of life and mental health**

Health-related quality of life was self-assessed using the standardised questionnaire Short Form 36, Physical Component Summary (SF-36 PCS) and Mental Health Component Summary (MCS) Scale, Hospital Anxiety and Depression Scale, anxiety subscale (HADS-A) and depression subscale (HADS-D), and HeartQol. Questionnaires were assessed at baseline two-five days after surgery and, one, four, six, 12 and 24 months after surgery.

**Register based outcomes**

The composite outcome of readmission and emergency room contacts and mortality were chosen for one combined outcome because the mortality rates in this population is very low.

**Readmission and emergency room contacts**

All hospital contacts including elective and acute hospital readmissions and emergency room contacts were retrieved from The Danish National Patient Register [18], which is a nationwide register with national coverage and none lost to follow-up. A readmission was any registration in The Danish National Patient Register according to the administrative coding. For this study we studied overall readmissions, acute and elective readmissions, and emergency room contacts.
Mortality
Vital status was retrieved from The Danish Civil Registration System [19]. This is a nationwide register with none lost to follow up. Data on mortality were available for all individuals. Mortality was all-cause mortality.

Statistical analyses
Baseline characteristics were compared using Students t-test and X^2 tests. Survival analysis was used to investigate the effect of CR participation and readmission, mortality and emergency room contacts. To limit the possibility of competing risk of death for some of the analyses, overall readmission and mortality were combined. Time to first overall readmission or mortality (combined), acute readmission, elective readmission, emergency room contacts and mortality was analysed using a Kaplan–Meier survival plot. Primary analysis compared intervention to controls over a 24 months’ time period. In sub-analyses, differences were compared at 3, 6, 12 and 18 months.

The mixed model with repeated measures (MMRM, proc mixed) was used for continuous outcomes (physical capacity and self-reported outcomes). This model assumes normally distributed residuals. All data were normally distributed thus transformation was not necessary. In the MMRM, correlation within the individual patient was assumed, but not between patients. The fixed effects for physical capacity were randomization group, time, interaction between random and time and LVEF. This was chosen initially as we would expect patients to have clinically different phenotypes according to LVEF.

All analyses were intention to treat and adjusted for the stratification variable LVEF. HADS probability of anxiety or depression score (cut-off at ≥8 on the two scales) was dichotomised and analysed as binary outcomes using mixed logistic regression model [20,21]. Data were analysed using SAS V.9.3 (SAS Institute, Cary, NC, USA), and SAS Enterprise vs. 7.2 and a statistical significance level set at 0.05.

Patient and public involvement
Patients were involved during the trials period in in several ways. Before initiating the trial, a qualitative interview study was performed to in depth investigate patients’ needs after heart valve surgery, in 2012 before initiating the clinical trial to properly tailor the intervention for the patients’ needs. During the randomized trial in 2012–2014 and after, patients were involved mainly through the patient reported outcome measures at the points of questionnaire measurements. After the intervention was finished in 2015, two qualitative interview studies were conducted, to evaluate patients’ experiences of participating in the trial.

Finally, after the long-term follow up measurements was finished at 12 months clinical visits, all patients were invited to a symposium together with researchers in 2016. Research findings was presented for the patients and the press, and patients had the opportunity to question the trial findings and with the researchers evaluate the experience of participating in the intervention, and further make proposals for further research.

Results
Study flow and baseline characteristics
A total of 901 patients were screened for the initial study; 546 were eligible, and of those 153 gave written informed consent for participation and were randomized to control (n = 75) and intervention (n = 72). Patients from Greenland and The Faroe Islands could not be followed in the registers for either readmission or mortality as the registers only includes Danish citizens. Thus, data are missing for 13 patients. Of the participants, 76% (n = 57, intervention group) and 65% (n = 47, control group) completed 12 months physical testing, and 79% (n = 59) and 78% (n = 56) completed health-related quality of life questionnaire (Figure 1).

Baseline characteristics is summarized in Table 1. The included population was 76% men, mean age 62 years, 62% with aortic valve surgery, 36% with mitral valve surgery or 2% with tricuspid/pulmonary valve surgery. NYHA class ranged from I to IV, with evidence of few comorbidities and a low mean EuroSCORE of 0.96 and 1.13 for the rehabilitation and control group, respectively. Almost one fourth of patients had clinically relevant symptoms of anxiety at baseline (HADS A ≥ 8).

Outcomes
Physical capacity
Over the 12 months period, an increase in physical capacity measured by VO_2peak (ml/min/kg) was found in both groups. The difference was statistically significantly between groups (p = .01). After 4 months an effect over time of the intervention in favour of the intervention group (p = .045) was found. After 12 months, there was no effect for the absolute values between groups (p = .069) (Table 2).

Both intervention and control group improved from baseline to 12 months in 6MWT mean of 50 meters and in the sit-to-stand test improvement of 2 repetitions, but with no statistically significant differences of the effect over time between groups (p for interaction 0.95 vs 0.96 for 6MWT and sit to stand, respectively) (Table 2).

Health related quality of life
There was no statistically significant differences of SF-36 MCS, PCS, HADS or HeartQoL between groups (Table 3) at 24 months. HADS-A scores were convincingly high at baseline (intervention and control: 17% vs 14%) but decreasing over time. The greatest improvement was from 0 to 4 months. Thereafter a ceiling effect of all patient reported outcomes was found, with no difference between groups of the intervention over time after 24 months (p for interaction non-significant for all measures) (Table 3).
Readmission and mortality

At 24 months, 3% patients in both groups had died. A plot of the combined cumulative incidences of overall readmission and mortality (Kaplan Meyer curves) showed that 68% patients in the intervention group and 75% in the control group had been readmitted or died after 24 months providing a non-statistically significant difference in overall readmissions and mortality between groups (p for log rank = 0.100) (Figure 2).

Favouring the intervention group sub-analyses showed statistically significant differences in combined readmission and mortality rate at 3 months (38% vs 56%, log rank test
95% CI: 95% Confidence Interval, m: Meter, n: number of repetitions.

difference (log rank test p = .024) with lower readmission and mortality rates in the intervention group (Figure 2). At 18 months, there were no significant difference (log rank test p = .056).

In acute and elective readmissions, no statistically significant differences were seen in favour of the intervention group after 24 months (p for log rank = .247 and p for log rank = .820, respectively). In the intervention group, 60% of patients had an acute readmission and 25% an elective readmission after 24 months. Similar numbers were 64% and 26% for controls (Figure 2).

Sub-analyses revealed statistically significant differences at 3 months in acute readmissions in favour of the intervention group (33% vs 52%, log rank test p = .021). For elective readmissions, sub-analyses revealed no differences even at additional time points.

**Emergency room contacts**

We found that 47% of patients in the intervention group and 40% in the control group had emergency room contacts, with no statistically significant differences after 24 months (Figure 2) or at earlier time points.

**Discussion**

Using long-term data from the randomised CopenHeartVR trial, in patients after heart valve surgery an effect up to 4 months on physical capacity and up to 12 months on readmissions in the CR group compared with control was demonstrated. There were no long-term effects after 2 years. The data used are from the largest randomised clinical trial to date regarding long-term effects of CR after heart valve surgery.

**Physical outcomes and health related quality of life**

There was no statistically significant effect of the intervention after 12 months on physical outcomes or after 24 months on health-related outcomes. However, there were differences in change over time, with the intervention group having at steeper slope from 1 to 4 months but at 12 month

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**Table 1. Baseline characteristics.**

| Variable                        | CR (n = 72) | Control group (n = 75) |
|---------------------------------|-------------|------------------------|
| Male sex, n (%)                 | 59 (82)     | 53 (71)                |
| Age, years (±SD)                | 62.0 (11.5) | 61.0 (9.9)             |
| Aortic valve surgery, n (%)     | 46 (64)     | 45 (60)                |
| Mitral valve surgery, n (%)     | 27 (38)     | 26 (35)                |
| Pulmonary and tricuspid valve surgery, n (%) | 1 (1.4) | 2 (3) |
| Symptoms prior to surgery, n (%) | 66 (92)    | 69 (92)                |
| NYHA class I-II, n (%)          | 53 (74)     | 52 (69)                |
| NYHA class III-IV, n (%)        | 19 (26)     | 23 (31)                |
| LVEF, mean (±SD)                | 35 (9.6)    | 54 (10.2)              |
| Preoperative LVEF ≥45%, n (%)   | 64 (89)     | 64 (85)                |
| EuroSCORE II                    | 1.13 (0.78) | 0.96 (0.58)            |
| Body mass index, mean (±SD)     | 26.2 (4.2)  | 26.1 (3.9)             |

**Table 2. Physical tests outcomes.**

| Variable                        | 1 month | 4 months | 12 months | 1 month | 4 months | 12 months | Interaction* p-value |
|---------------------------------|---------|----------|-----------|---------|----------|-----------|----------------------|
| Peak VO2 (ml/min/kg)            | 21.8 (20.1–23.5) | 25.5 (23.6–27.3) | 25.5 (23.5–27.7) | 21.7 (20.0–23.4) | 23.2 (20.9–25.4) | 26.2 (23.3–29.0) | .01                   |
| Max Watt                        | 134.6 (123.9–145.2) | 167.6 (153.0–181.1) | 171.6 (154.8–188.3) | 134.3 (122.7–145.9) | 152.6 (138.1–167.1) | 161.6 (144.1–179.2) | .10                   |
| Six minutes’ walk test (m)      | 546.1 (523.5–568.8) | 597.4 (572.6–622.3) | 601.5 (574.9–628.1) | 542.8 (520.7–564.8) | 594.3 (572.1–616.5) | 596.6 (569.7–623.5) | .95                   |
| Sit to stand test (n)           | 15.0 (13.9–16.0) | 17.4 (16.1–18.7) | 17.1 (16.1–19.1) | 15.4 (14.2–16.3) | 17.5 (16.1–19.0) | 17.9 (16.1–19.6) | .96                   |

*p-values for intervention x time interactions adjusted for LVEF.
95% CI: 95% Confidence Interval, m: Meter, n: number of repetitions.
Table 3. Patient-reported outcomes over time from baseline to 24 months.

| Variables | CR Control group |
|-----------|------------------|
|          | Baseline 1 month 4 months 6 months 12 months 24 months Baseline 1 month 4 months 6 months 12 months 24 months | Interaction* |
| SF-36 Mean (95% CI) | Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) Mean (95% CI) |
| Mental component | 49.1 (46.9–51.3) 50.3 (47.8–52.8) 51.3 (50.9–52.6) 57.6 (55.9–59.2) 51.3 (50.3–57.0) 55.0 (53.5–57.7) 51.3 (50.9–56.2) 53.9 (51.3–56.4) 55.1 (53.1–57.0) 57.6 (55.9–59.2) 51.3 (50.9–56.2) 55.0 (53.5–57.7) |
| Physical component | 40.7 (38.5–42.9) 40.0 (38.3–41.7) 50.4 (48.3–52.5) 51.2 (49.2–53.3) 51.1 (49.0–53.2) 50.1 (48.1–52.1) 40.9 (38.3–41.7) 40.0 (38.3–41.7) 51.0 (49.0–53.0) 52.2 (50.3–54.2) 52.0 (50.1–53.3) 50.7 (48.1–53.3) |
| HADS Number (%) | Number (%) Number (%) Number (%) Number (%) Number (%) Number (%) Number (%) Number (%) Number (%) Number (%) |
| AHADS/C21 | 8 (17.9) 8 (12.3) 11 (16.9) 7 (10.8) 7 (11.1) 4 (6.6) 14 (21.2) 7 (11.5) 5 (8.5) 7 (12.1) 5 (8.9) 8 (14.8) |
| DHEADS | 2 (2.9) 2 (8.2) 3 (4.6) 6 (4.6) 6 (4.8) 6 (4.6) 5 (7.6) 5 (6.6) 5 (7.6) 2 (3.3) 2 (1.8) 2 (1.8) |
| HeartQol Global | 1.5 (1.3–1.7) 2.0 (2.4–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 1.5 (1.3–1.7) 1.5 (1.3–1.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) |
| HeartQol Emotional | 2.0 (1.8–2.1) 2.6 (2.4–2.7) 2.7 (2.5–2.8) 2.7 (2.5–2.8) 2.7 (2.5–2.8) 2.7 (2.5–2.8) 1.9 (1.7–2.1) 1.9 (1.7–2.1) 2.7 (2.5–2.8) 2.7 (2.5–2.8) 2.7 (2.5–2.8) 2.7 (2.5–2.8) |
| HeartQol Physical | 1.3 (1.1–1.5) 2.5 (2.4–2.7) 2.6 (2.4–2.7) 2.5 (2.4–2.7) 2.5 (2.4–2.7) 2.5 (2.4–2.7) 1.3 (1.1–1.5) 1.3 (1.1–1.5) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) 2.6 (2.5–2.7) |

*P-values for interaction between intervention and time in mixed model adjusted for LVEF at 4 months. 95% CI: 95% Confidence Interval, SF-36: Short Form 36, HADS: Hospital Anxiety and Depression Scale, A: Anxiety, D: Depression.
usual care [11, 30]. The data demonstrated a reduction in the composite endpoint of readmission and mortality to 23% compared with 37% for a historical control group. Economic analyses also showed that the intervention group costed €793 ($83, p < .001) less per patient [10]. Interestingly, a Norwegian study found that a 24/7 telephone intervention after aortic valve surgery did not decrease readmission rates but measured reduced levels of anxiety [31].

In this study, we did not intend to investigate clinical follow up but both our findings and the INVOLVE study from a Danish setting argues that clinical follow-up and CR is essential in the months post-surgery, to obtain less readmissions.

Recent descriptions of valve clinics suggest that follow up is organized around a valve centre model, with a multidisciplinary team [4,6]. These are new approaches to meet unmet needs, but with less focus on post-valve surgery care. According to our data, CR after heart valve surgery should probably be considered, but specifically tailored for the individual patient.

In future studies, patients should be stratified according to deconditioning, clinical baseline phenotype and prognosis when planning follow-up and clinical CR after valve surgery and stratified according to complexity of the valve disease. CR after heart valve surgery should be driven by relevant patient-reported outcomes, predictors of readmission, and clinical outcomes (atrial fibrillation, heart failure, pericardial effusions, pleural effusions and typical complications of surgery, return to work and sick leave). These findings also invite to study barriers to CR enrolment, and to base studies on observational field studies including patient public involvement. Finally, well conducted multicentre trials assessing the cost-effectiveness and clinical relevance of exercise-based CR after valve surgery including both transcatheter based interventions and after open heart valve surgery [32] are needed, before CR can be applied as a policy recommendation.

**Study limitations**

This study is based on pre-planned secondary data collected to perform explorative long-term analyses from an RCT, and thus, the sample size calculation was based on the...
primary outcomes measured after four months, and not powered to estimate mortality or readmission. Further, blinding to the intervention in CR trials is not possible, but outcome assessment and statistical analyses were blinded to intervention group. Self-reported data are subjective by nature, and drift in register coding might exist. Further, physical examinations are subject to physiological changes leading to day-to-day and time-of-day variations.

Conclusions

Undertaking exercise-based CR after heart valve surgery reduces readmissions and mortality combined up to 12 months after surgery despite lack of improvement in exercise capacity, physical and mental health at 12 months and with no effect after 24 months. Exercise-based CR can ensure short term benefits in terms of physical capacity, and lower readmission within a year, but more research is needed to sustain these effects over a longer time period. These considerations should be included in the management of patients after heart valve surgery.

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References

[1] Coffey S, Cairns BJ, Iung B. The modern epidemiology of heart valve disease. Heart. 2016;102(1):75–85.
[2] Vahanian A, Breyer D, Praz F, ESC/EACTS Scientific Document Group, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. Eur Heart J. 2022;43(7):561–632.
[3] Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;70(2):252–289.
[4] Chambers JB, Prendergast B, Iung B, et al. Standards defining a ‘Heart Valve Centre’: ESC Working Group on Valvular Heart Disease and European Association for Cardiothoracic Surgery Viewpoint. Eur J Cardiothorac Surg. 2017;52(3):418–424.
[5] Chambers JB, Ray S, Prendergast B, et al. Specialist valve clinics: recommendations from the British Heart Valve Society working group on improving quality in the delivery of care for patients with heart valve disease. Heart. 2013;99(23):1714–1716.
[6] Lancellotti P, Rosenhek R, Pibarot P, et al. ESC working group on Valvular Heart Disease position paper–heart valve clinics: organization, structure, and experiences. Eur Heart J. 2013;34(21):1597–1606.
[7] Danielsen SO, Moons P, Sandven I, et al. Thirty-day readmissions in surgical and transcatheter aortic valve replacement: A systematic review and meta-analysis. International Journal of cardiology. 2018;268:85–91.
[8] Kwok CS, Balacumaraswami L, Mamas MA. Should we implement interventions to reduce readmissions in open heart valve surgery? Int J Cardiol. 2019;289:50–51.
[9] Sibilitz KL, Berg SK, Thygesen LC, et al. High readmission rate after heart valve surgery: A nationwide cohort study. International Journal of cardiology. 2015;199:96–104.
[10] Hansen TB, Zwisler AD, Berg SK, et al. Exercise-based CR after heart valve surgery: cost analysis of healthcare use and sick leave. Open Heart. 2015;2(1):e000288.
[11] Borregaard B, Dahl JS, Riber LPS, et al. Data on an intervention to reduce readmissions after open heart valve surgery. Data Brief. 2019;24:103926.
[12] Anderson L, Thompson DR, Oldridge N, et al. Exercise-based CR for coronary heart disease. Cochrane Database Syst Rev. 2016;67(1):1–12.
[13] Sibilitz KL, Berg SK, Tang LH, et al. Exercise-based CR for adults after heart valve surgery. Cochrane Database Syst Rev. 2016;3:CD010876.
[14] Sibilitz KL, Berg SK, Rasmussen TB, et al. CR increases physical capacity but not mental health after heart valve surgery: a randomised clinical trial. Heart. 2016;102(24):1995–2003.
[15] Anderson L, Taylor RS, CR for people with heart disease: an overview of Cochrane systematic reviews. Cochrane Database Syst Rev. 2014;12:CD011273.
[16] Lund K, Sibilitz KL, Berg SK, et al. Physical activity increases survival after heart valve surgery. Heart. 2016;102(17):1388–1395.
[17] Sibilitz KL, Berg SK, Hansen TB, et al. Effect of comprehensive CR after heart valve surgery (CopenHeartVR): study protocol for a randomised clinical trial. Trials. 2013;14:104.
[18] Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. Scand J Public Health. 2011;39(7 Suppl):30–33.
[19] Pedersen CB. The Danish civil registration system. Scand J Public Health. 2011;39(7 Suppl):22–25.
[20] Christensen AV, Dixon JK, Juel K, et al. Psychometric properties of the Danish Hospital Anxiety and Depression Scale in patients with cardiac disease: results from the DenHeart survey. Health Qual Life Outcomes. 2020;18(1):9.
[21] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361–370.
[22] Uddin J, Zwisler AD, Lewinter C, et al. Predictors of exercise capacity following exercise-based rehabilitation in patients with coronary heart disease and heart failure: A meta-regression analysis. Eur J Prev Cardiol. 2016;23(7):683–693.
[23] Borregaard B. Sociodemographic-, clinical- and patient-reported outcomes and readmission after heart valve surgery. J Heart Valve Dis. 2018;27(1):78–86.
[24] Christensen AV, Bjorner JB, Juel K, et al. Increased risk of mortality and readmission associated with lower SF-12 scores in cardiac patients: results from the national DenHeart study. Eur J Cardiovasc Nurs. 2019;18(4):330–338.
[25] Christensen AV, Juel K, Ekholm O, et al. Significantly increased risk of all-cause mortality among cardiac patients feeling lonely. Heart. 2020;106(2):140–146.
[26] Bachmann JM, Duncan MS, Shah AS, et al. Association of CR With Decreased Hospitalizations and Mortality After
Ventricular Assist Device Implantation. JACC Heart Failure. 2018;6(2):130–139.

[27] Patel DK, Duncan MS, Shah AS, et al. Association of CR with decreased hospitalization and mortality risk after cardiac valve surgery. JAMA Cardiol. 2019;4(12):1250.

[28] Goel K, Pack QR, Lahr B, et al. Cardiac rehabilitation is associated with reduced long-term mortality in patients undergoing combined heart valve and CABG surgery. Eur J Prev Cardiol. 2015;22(2):159–168. Feb

[29] Pack QR, Lahr BD, Squires RW, et al. Survey reported participation in CR and survival after mitral or aortic valve surgery. Am J Cardiol. 2016;117(12):1985–1991.

[30] Borregaard B, Dahl JS, Riber LPS, et al. Effect of early, individualized and intensified follow-up after open heart valve surgery on unplanned cardiac hospital readmissions and all-cause mortality. Int J Cardiol. 2019;289:30–36.

[31] Danielsen SO, Moons P, Sandvik L, et al. Impact of telephone follow-up and 24/7 hotline on 30-day readmission rates following aortic valve replacement -A randomized controlled trial. Int J Cardiol. 2020;300:66–72.

[32] Anayo L, Rogers P, Long L, et al. Exercise-based CR for patients following open surgical aortic valve replacement and transcatheter aortic valve implant: a systematic review and meta-analysis. Open Heart. 2019;6(1):e000922.