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ORIGINAL ARTICLE

Long-term effects of cardiac rehabilitation after heart valve surgery - results from the randomised CopenHeart$_{VR}$ trial

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ABSTRACT

Aims. The CopenHeart$_{VR}$ 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 he CopenHeart$_{VR}$ Trial we investigated long-term effects on physical capacity, mental and physical health and effect on mortality and readmission rates as pre-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 (VO_2 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 VO_2 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.

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Heart valve surgery; cardiac rehabilitation; clinical follow-up; physical exercise; heart valve clinic

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 va1ve 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

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†This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

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 CopenHeart$_{VR}$ 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 CopenHeart$_{VR}$ 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 CopenHeart$_{VR}$ 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 CopenHeart$_{VR}$ 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 (VO_2 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.

Thee 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 $\geq$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 $A \geq 8$).

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 convincinhigh 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).

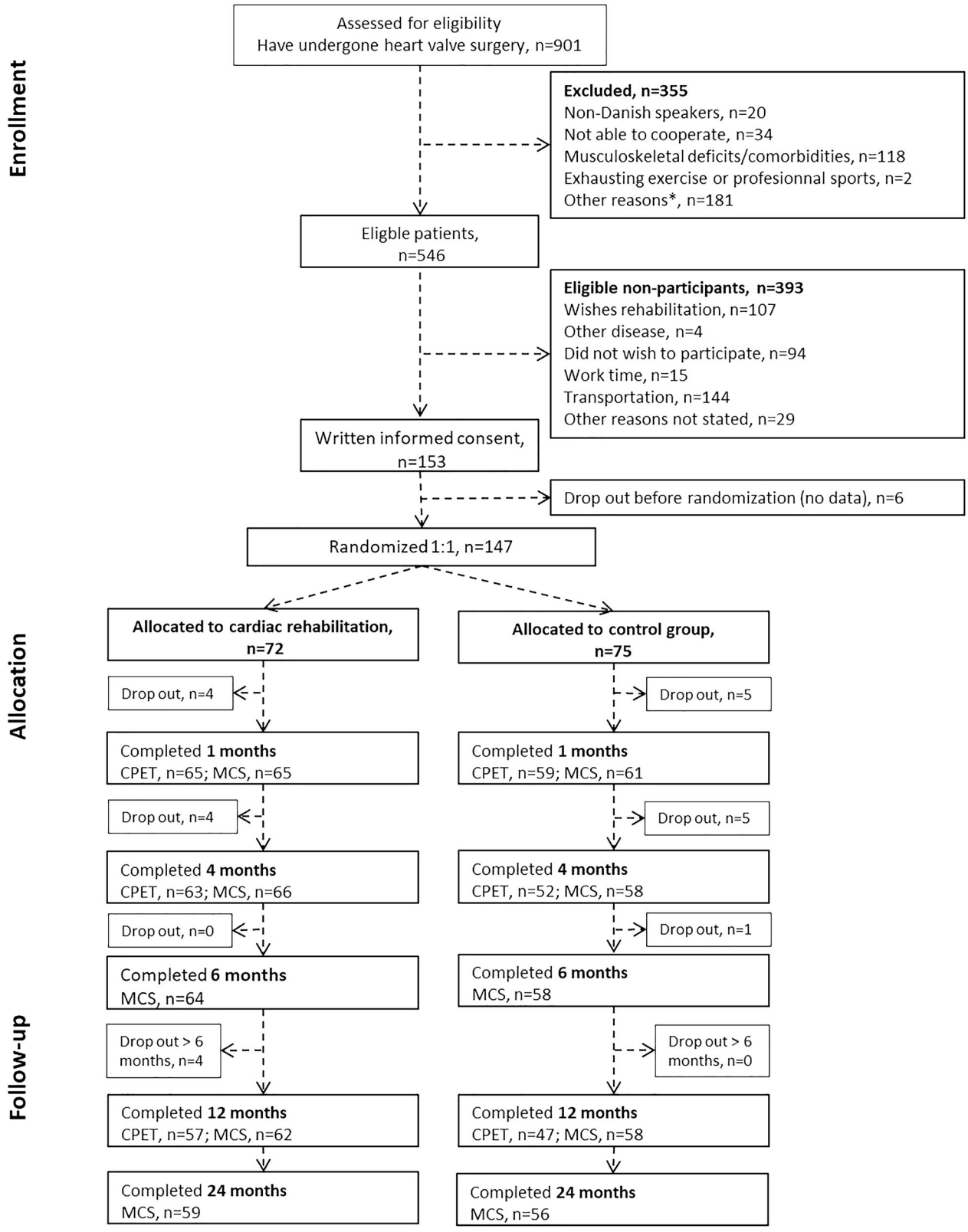

Figure 1. Consort flow chart of study participants. CPET: Cardiopulmonary Exercise Test, MCS: Short Form 36 Mental Health Component Summary.

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

Table 1. Baseline characteristics.

	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)
Pulmonal and tricuspid valve surgery, *n* (%)	1 (1.4)	2 (3)
Symptoms prior to surgery[a], *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)	55 (9.6)	54 (10.2)
Preoperative LVEF $\geq$ 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)
Medical history		
Atrial fibrillation, *n* (%)	15 (21)	64 (85)
Hypertension, *n* (%)	28 (39)	34 (45)
Diabetes mellitus, *n* (%)	2 (3)	7 (9)
Dyslipidemia, *n* (%)	1(1.4)	1 (1.3)
Current smoking, *n* (%)	7 (10)	5 (7)
Medication[†]		
Beta-blocker, *n* (%)	27 (38)	28 (37)
ACE inhibitor, *n* (%)	24 (33)	19 (25)
Amiodarone, *n* (%)	21 (29)	21 (28)
Antiarrhythmics, *n* (%)[‡]	17 (24)	9 (12)
Vitamin K antagonists, *n* (%)	54 (75)	57 (76)
ASA, *n* (%)	21 (29)	22 (29)
Statin, *n* (%)	26 (36)	27 (36)

NYHA, New York Heart Association; LVEF, Left Ventricular Ejection Fraction; EuroSCOREII, European System for Cardiac Operative Risk Evaluation. [a]Symptoms prior to surgery are self-reported and include dyspnoe, angina pectoris, palpitations, decreased physical activity level; HADS, A, Hospital Anxiety and Depression Scale – Anxiety domain; HADS, D, Hospital Anxiety and Depression Scale – Depression domain; [†]Medication status is at discharge and drawn from the electronic medical records; [‡]Ca^{2+}antagonist or Digoxin.

Table 2. Physical tests outcomes.

Variables	CR			Control group			Interaction[a]
	1 month Mean (95% CI)	4 months Mean (95% CI)	12 months Mean (95% CI)	1 month Mean (95% CI)	4 months Mean (95% CI)	12 months Mean (95% CI)	*p*-value
Peak VO_2 (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

[a]*p*-values for intervention x time interactions adjusted for LVEF.
95% CI: 95% Confidence Interval, m: Meter, n: number of repetitions.

$p = .019$), 6 months (43% vs 60%, log rank test $p = 0.024$) and 12 months (53% vs 68%, log rank test $p = .031$) 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 $CopenHeart_{VR}$ 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

Table 3. Patient-reported outcomes over time from baseline to 24 months.

	CR						Control group						
Variables	Baseline	1 month	4 months	6 months	12 months	24 months	Baseline	1 month	4 months	6 months	12 months	24 months	Interaction[a]
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 scale	49.1 (46.9–51.3)	50.3 (47.8–52.8)	54.7 (52.6–56.7)	53.6 (50.9–56.2)	55.1 (53.1–57.0)	55.5 (53.5–57.5)	49.7 (47.1–52.4)	50.0 (47.3–52.8)	53.9 (51.3–56.4)	55.1 (52.8–57.5)	55.5 (53.3–57.7)	54.0 (51.2–56.9)	.58
Physical component scale	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 (38.3–43.6)	40.0 (38.0–42.1)	51.0 (49.0–53.0)	52.2 (50.3–54.2)	52.0 (50.1–53.8)	50.7 (48.1–53.3)	.99
HADS	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	
HADS $A \geq 8$	17 (23.9)	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)	.29
HADS $D \geq 8$	2 (2.9)	4 (6.2)	3 (4.6)	4 (6.2)	3 (4.8)	4 (6.6)	5 (7.6)	4 (6.6)	2 (3.4)	2 (3.5)	1 (1.8)	5 (9.3)	.66
HeartQoL	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)	
HeartQoL Global	1.5 (1.3–1.7)	–	–	2.6 (2.4–2.7)	2.6 (2.5–2.7)	2.6 (2.5–2.7)	1.5 (1.3–1.7)	–	–	2.6 (2.5–2.7)	2.6 (2.5–2.8)	2.6 (2.4–2.7)	.73
HeartQoL Emotional	2.0 (1.8–2.1)	–	–	2.6 (2.4–2.7)	2.7 (2.5–2.8)	2.7 (2.6-2.8)	1.9 (1.7–2.1)	–	–	2.7 (2.5–2.8)	2.7 (2.6–2.8)	2.7 (2.5–2.8)	.45
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)	1.3 (1.1–1.5)	–	–	2.6 (2.5–2.7)	2.6 (2.5–2.8)	2.5 (2.4–2.7)	.89

[a]P-va lues 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.

both groups had equal values for VO2. This indicates that the control group recovers spontaneously. A clinically relevant difference is considered an improvement of 3,5 ml/kg/min [22], and this is achieved in both groups over the first year.

Physical capacity after valve surgery is a predictor of mortality[16], but with an equal mortality rate in both groups such link with CR participation could not be established. Several studies have found that health related outcomes are associated with readmission and mortality in Danish cardiac populations [9,23,24]. Also, feeling lonely is a strong predictor of worse outcome [25]. The explanation for our findings, might be that the trial was not designed to capture these outcomes at 24 months. Speculations are that the CR program may be too short to capture any effects long-term, may not be appropriate, or should be repeated yearly and with a greater focus on long-term management at home to measure any long term effects.

Readmission and mortality and cardiac rehabilitation

There was a reduction at intermediate time points in readmission and mortality but no effect at 24 months. Due to the low number of mortality, differences are mainly driven by readmission. In patients with ischemic heart disease previous evidence is strong in demonstrating that CR reduces cardiovascular readmissions and mortality at 12 months follow-up [12]. In other populations such as patients with heart failure and patients with device implantations, similar findings exist [26]. In a Cochrane review regarding the effect of CR after valve surgery, readmission and mortality could not be investigated due to limited data [13]. One recent cohort study by Patel and colleagues found that among 41,369 Medicare beneficiaries, 43.2% who had valve surgery patients enrolled in CR programs, and that CR enrolment was associated with 34% reduction in hospitalizations within one year of discharge, and with a 4.2% absolute decrease in 1-year mortality risk [27]. In line with this, a study investigating a smaller cohort of 201 patients with combined valve surgery and coronary artery bypass grafting reported a significant survival benefit of CR participation [28]. However, a survival benefit of CR could not be confirmed in a survey study from 2013 [29].

In conclusion, CR is now in several studies associated with a lower short-term readmission rate, but with no change in mortality. Yet, mortality rate is so low that it does not constitute the primary reason for providing CR to this population"

Interventions to reduce readmission after heart valve surgery and procedures

A recent study identified predictors of readmission after heart valve surgery and found several outcomes associated with worse outcomes emphasising the need for individualised follow-up [23]. This was focus for the INVOLVE trial applying an intensive, individually stratified follow-up program in a dedicated heart valve clinic as a supplement to

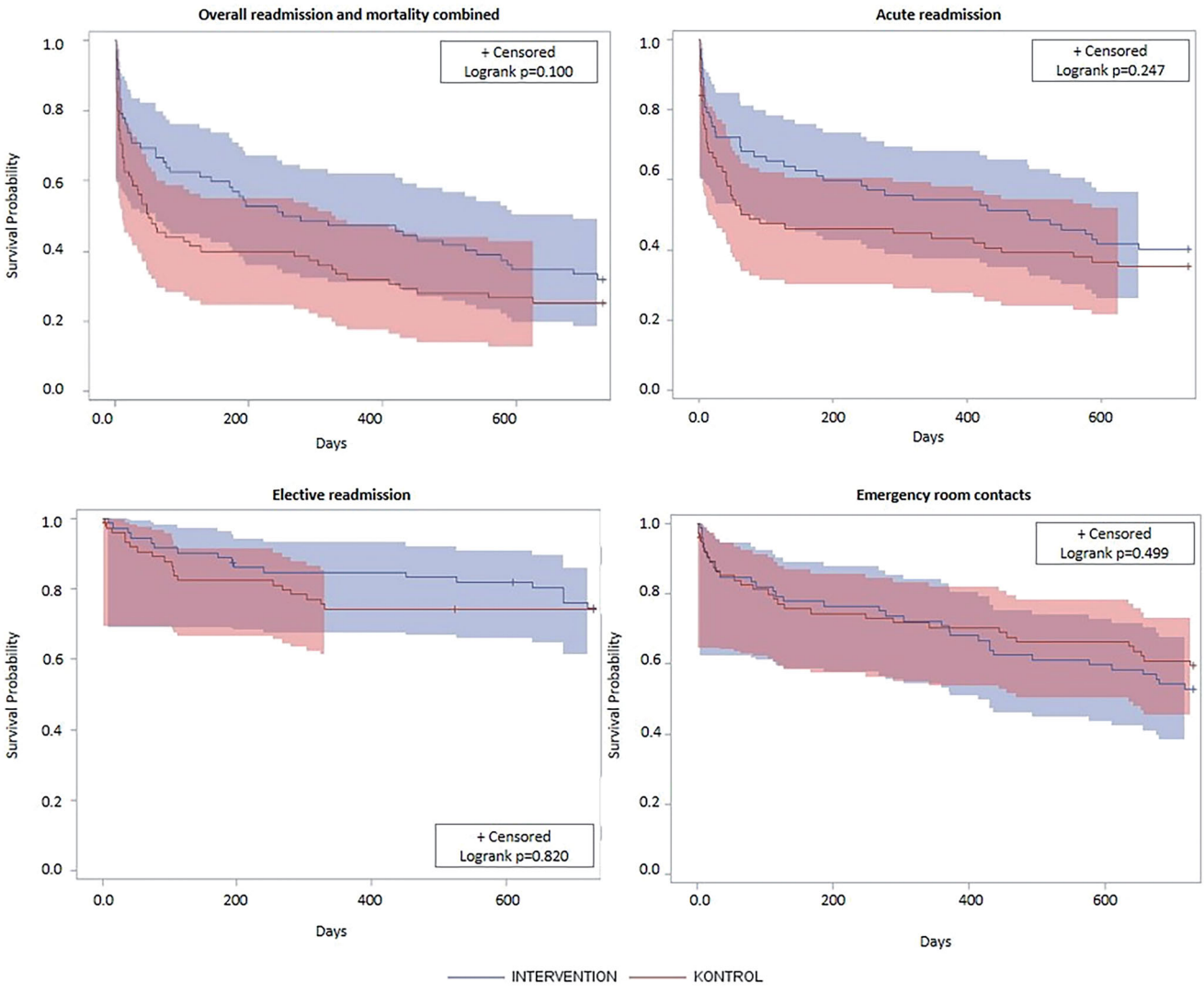

Figure 2. Kaplan-Meier survival plots comparing 1) overall readmission and mortality combined, readmissions divided into 2) acute and 3) elective readmission, and 4) emergency room contacts between intervention and control group over 24 months. Log rank test presented is for 24 months in all plots. The blue and red areas llustrate the 95% confidence intervals for each Kaplan-Meier curves.

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 ($p < .001$) 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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