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The Effect of Teleprehabilitation on Adverse Events After Elective Cardiac Surgery

A Randomized Controlled Trial

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ABSTRACT

BACKGROUND Patients scheduled for cardiac surgery and procedures often present with modifiable risk factors for adverse perioperative outcomes. Prehabilitation has shown potential to enhance mental and physical fitness; however, its effect on clinical cardiovascular endpoints in this population has not been studied.

OBJECTIVES The current trial was designed to evaluate the effect of a personalized multimodal teleprehabilitation on the incidence of composite endpoint on major adverse cardiovascular events in patients scheduled for elective cardiac surgery.

METHODS In a multicenter randomized controlled trial, 394 patients awaiting elective cardiac surgery and procedures were enrolled. Of these, 197 patients were randomized to an online multimodal personalized teleprehabilitation program through shared decision-making by a multidisciplinary team, and 197 were assigned to a control group. The primary outcome was major adverse cardiovascular events (ie, cardiovascular death, myocardial infarction, stroke, hospitalization for heart failure or other life-threatening cardiac events, and earlier or repeated intervention), as measured from the randomization until 1-year postoperatively. All events were adjudicated by a blinded event committee. Secondary outcomes included length of hospital stay, postoperative complications, quality of life, adherence to the program, and effect on the incidence of modifiable risk factors. Sensitivity analyses of the primary outcome were conducted adjusting for baseline characteristics to evaluate the consistency of treatment effects.

RESULTS From randomization until 1 year postoperatively, the primary endpoint occurred in 33 patients (16.8%) in the teleprehabilitation group and 50 patients (25.5%) in the control group (difference 8.8%; 95% CI: 0.7%-16.8%; $P = 0.032$). This difference was primarily driven by a reduction in hospitalizations, and the sensitivity analyses showed that treatment effect was mainly in the patients undergoing a cardiac surgery rather than transcatheter procedures with adjusted OR of 0.54 (95% CI: 0.30-0.96; $P = 0.035$). Teleprehabilitation also reduced the incidence of active smokers, elevated pulmonary risk scores, and elevated depression scores. There was no significant difference in postoperative length of hospital stay, occurrence of postoperative complications, physical fitness, incidence of obesity, or malnutrition.

CONCLUSIONS Multimodal personalized teleprehabilitation resulted in a clinically relevant and statistically significant reduction of the primary endpoint in patients undergoing cardiac surgery. (Digital Cardiac Counseling Trial: DCC Trial [DCC]; NCT04393636) (JACC. 2024;■:■-■) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

LVEF = left ventricular ejection fraction

MACE = major adverse cardiovascular events

MIP = maximal inspiratory pressure

TAVR = transcatheter aortic valve replacement

In recent decades, the cardiac surgery population has progressively aged and presented with more comorbidities and risk factors, thereby increasing the risk of adverse perioperative outcomes.[1] Many of these risk factors are modifiable through preoperative interventions such as exercise training,[2,3] smoking cessation,[4,5] and psychological support.[6] A preoperative assessment offers the opportunity to identify these modifiable risk factors and guide subsequent personalized preventive interventions during the preoperative period.

Prehabilitation in patients scheduled for cardiac surgery has demonstrated the potential to enhance mental and physical fitness, consequently improving postoperative outcomes such as shortened hospital stays, reduced postoperative complications, and enhanced health-related quality of life.[7-11] However, no research in this population has studied the effect of prehabilitation on the incidence of clinical cardiovascular endpoints.

Previous research in the field of cardiac prehabilitation has primarily focused on the delivery of center-based programs consisting of unimodal interventions. However, optimal prehabilitation programs should include all core components and be personalized to each patient's risk profile and preferences through shared decision-making. Barriers to the adoption of center-based programs, such as lack of flexibility and limited accessibility, might be overcome by teleprehabilitation, which not only addresses these barriers but also has the potential to increase cost-effectiveness.[12,13]

To address this gap, the DCC (Digital Cardiac Counseling) trial was designed to compare the effectiveness of a personalized multimodal teleprehabilitation program against a control group receiving no teleprehabilitation in reducing the incidence of major adverse cardiovascular events (MACE) in patients scheduled for elective cardiac surgery and procedures.

METHODS

TRIAL OVERSIGHT. The DCC trial was an investigator-initiated multicenter, randomized, unblinded, controlled trial that included patients from the Maastricht University Medical Center and multiple referral centers, with the intervention (teleprehabilitation) conducted remotely in patients' home environments. The trial design has been published previously.[14] In brief, an open-label multicentered randomized controlled trial was performed that compared an intervention group receiving a multimodal teleprehabilitation program, personalized to each patient's risk profile and preferences guided by shared decision-making, with a control group in patients awaiting elective cardiac surgery. The actual prehabilitation program was led by a multidisciplinary team, including a cardiologist, nurses, physiotherapists, a psychological counselor, and dietitians and was remotely supervised with video consultations. The trial protocol, available in the Supplemental Appendix, was approved by the Medical Ethical Committee of Maastricht University Medical Center/Maastricht University (NL73754.068.20/METC20-028). The trial was independently monitored and audited by the Clinical Trial Center Maastricht, and performed in accordance with the principles of the Declaration of Helsinki. The authors assume responsibility for the accuracy and completeness of the data and analyses, as well as for the fidelity of the trial and this report to the protocol.

PATIENTS. Adult patients (age 18 years or older) from multiple referral centers that were discussed at heart team at the Maastricht University Medical Center and scheduled for elective cardiac surgery, and procedures were assessed for study eligibility. The surgery needed to be scheduled at least 8 weeks after obtaining informed consent, allowing for a minimum prehabilitation period of 6 weeks. Patients were not excluded based on their primary cardiac pathology, surgery characteristics, or other comorbidities. The surgical treatment was performed by the Department of Cardiothoracic Surgery at the Maastricht University Medical Center, with 7 surgeons carrying out the cardiac surgery and procedures. All patients went through the same perioperative process with the same team. Within the department, there is subspecialization, with dedicated teams for specific

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treatments, such as those for mitral valve disease (minimally invasive and sternotomy), transcatheter procedures like transcatheter aortic valve replacement (TAVR), (minimally invasive) coronary disease, aortic surgery, and rhythm interventions. The trial included transcatheter procedures such as TAVR. Only patients who could not use a digital platform even with the help of an informal caregiver (eg, because of lack of internet access and/or digital literacy); patients with a language barrier (unable to speak or read Dutch at a sufficient level); and patients with interfering physical, psychiatric, or neurological conditions that made it impossible to complete the study procedures were excluded. Reasons and predictors for nonparticipation in the randomized trial were published previously.[15]

TRIAL PROCEDURES. Participants were randomly assigned in a 1:1 ratio to either the intervention group or to the control group. Randomization was performed, with the use of a web-based system, in permuted blocks, with block sizes of 4, 6, and 8, and stratified according to invasive vs minimally invasive surgery and the EuroSCORE II (0%-<2%, 2%-<5%, and ≥5%). All participants were given access to a customized digital environment on an exciting software framework (Medify BV). The platform was used to present personalized audio-visual information regarding the scheduled surgical procedure and hospital admission, to screen for the risk factors, to provide the personalized teleprehabilitation, and to do scheduled follow-ups. During the preoperative period, all patients were also remotely monitored for symptom progression based on their NYHA functional class, Canadian Cardiovascular Society (CCS) class, and COVID-19 symptoms according to the Dutch National Institute for Public Health and the Environment on a weekly basis through the platform. Patients showing symptom progression were reviewed with their referring cardiologists at different centers for potential adjustment of medical therapy or prioritization of their scheduled surgery. Follow-up was performed at 3 months, 6 months, and 1 year after the index surgery.

PERSONALIZED TELEPREHABILITATION PROGRAM. At baseline, all participants were screened for modifiable risk factors using patient-reported questionnaires. In the intervention group, the screening results were discussed with the patient and a case manager. Using shared decision-making, the teleprehabilitation program was then tailored to meet the specific needs and preferences of each patient. Participation in a given module was only possible if the screening for that module was positive. Patients in the intervention group could participate in 1 or more of the following 5 modules: functional exercise training, inspiratory muscle training, psychological support, nutritional support, and smoking cessation. Each module was supervised by health care professionals with expertise in cardiac rehabilitation. The modules were delivered through blended care, incorporating video consultations, telephone calls, and audiovisual instructions via the online platform. A brief description of each module is provided below; more detailed information is available in the trial design.[14]

Functional exercise training. Patients were screened for reduced physical fitness using a subset of the 36-item Short Form Health Survey (SF-36). In addition, 3 questions using a visual analogue scale (VAS) assessed the following: 1) difficulties in acknowledging physical limitations during daily activities; 2) awareness of physical boundaries; and 3) anxiety or fear related to physical exercise. A VAS score of ≥6 was considered positive and identified candidates for functional exercise training. The goal of this module was to promote preoperative physical activity, enhance physical fitness, increase knowledge and acceptance, and reduce anxiety related to physical exercise. Based on a metabolic equivalent score list for current activity levels, patients were advised by a physiotherapist to train 3 times per week in their home environment. The intensity of the training was adjusted during follow-up consultations using the Borg score of perceived exertion.[16]

Inspiratory muscle training. Patients were offered inspiratory muscle training when they had a pulmonary risk score ≥2, which assesses the risk of postoperative pulmonary complications.[16] The training aimed to increase inspiratory muscle strength, with sessions scheduled 5 times per week, twice daily. Each session consisted of 3 sets of 10 inspirations against resistance using the POWERbreathe device (POWERbreathe International Ltd, Southam). Training intensity was personalized using a predicted maximal inspiratory pressure (MIP), calculated from a regression formula that included sex, age, weight, and height provided by POWERbreathe. The intensity was adjusted during follow-up consultations according to the Borg score.

Psychological support. Patients with an elevated Hospital Anxiety and Depression Scale (HADS)[17] of ≥8 were offered psychological support by a psychological counselor. The goal of this module was to alleviate symptoms of anxiety and depression. The psychological support program was based on the Acceptance and Commitment Therapy philosophy and mindfulness techniques. It was delivered

through video consultations and psycho-education materials provided on the digital platform.

Nutritional support. Patients with obesity, defined as a body mass index (BMI) ≥30 kg/m^2, and those at risk of malnutrition, identified by a Malnutrition Universal Screening Tool (MUST) score ≥2,[18] were offered nutritional support by a dietician. The aim was to improve preoperative nutritional status. Patients with an elevated MUST score were screened for malnutrition and, if needed, treated with (protein-) enriched supplements based on the dietician's recommendations. The goal was not to promote extreme preoperative weight loss in patients with obesity.

Smoking cessation. Patients who smoked were offered a smoking cessation program led by a pulmonary care nurse, supported by video consultations and motivational enhancement techniques. If indicated, the program included nicotine replacement therapy or antidepressants.

OUTCOMES. The primary outcome was the composite endpoint of MACE (ie, cardiovascular death, myocardial infarction, stroke, hospitalization for heart failure or other life-threatening cardiac events, and earlier or repeated intervention as measured from inclusion until 1 year postoperative, or end of follow-up). Secondary outcomes were MACE during the preoperative and postoperative period, all-cause, cardiovascular, and COVID-19–related mortality, incidence of postoperative complications, postoperative length of hospital stay, and health-related quality of life, as measured with the EuroQol 5-dimensional 5-level questionnaire (EQ-5D-5L).[19] The EQ-5D-5L was assessed through an online patient-reported questionnaire, which was automatically transferred from the patient platform to the database.

For all patients, the overall incidence of modifiable risk factors was assessed at baseline and re-evaluated on the day of hospital admission before the index surgery or procedure. Patients who did not complete the baseline assessment were excluded from this analysis. Patients who failed to complete the assessment at hospital admission were still considered eligible for inclusion in this analysis, leading to missing data. All the assessments were completed by patients on the digital platforms and transferred directly into the database. For each module, we calculated the participation rate as a percentage of the eligible patients within the intervention group. We also reported the number of supervised consultations within each module and the duration of the preoperative period for each patient, categorized as <8 weeks or 8 weeks or longer from randomization to the time of index surgery. In cases where a scheduled surgery or procedure was canceled (eg, because of a change in the treatment plan), the cancellation date was used as the starting point for the 1-year follow-up to evaluate the effect of the teleprehabilitation program. Patients whose surgery was canceled were excluded from the analysis of preoperative period duration, length of hospital stay, and postoperative complications.

Socioeconomic status (SES) scores per neighborhood were obtained via Statistics Netherlands, which were measured based on household data regarding welfare, educational level, and labor participation. Scores range from −1 (lowest SES) to +1 (highest SES), where 0 is the average SES in the Netherlands.[20] All outcome definitions are specified in the Supplemental Data. Relevant source documents of all primary outcome events were collected for adjudication by a blinded independent events committee consisting of a senior academic cardiologist, cardiac surgeon, and neurologist.

STATISTICAL ANALYSIS. We expected that ∼20% of the patients in the control group would experience the primary outcome. A total of 197 patients were needed per group, or 394 in total, to be able to have 80% power to detect an absolute difference of 10% between groups using an alpha of 0.05. The principal analyses were performed in the intention-to-treat population, which included all patients according to the group to which they were randomly assigned, regardless of the treatment received. Postoperative length of hospital stay and the incidence of postoperative complications were only determined in patients who underwent cardiac surgery or procedure.

The difference in the occurrence of any MACE from inclusion until 1-year follow-up postoperatively between groups was tested using Pearson's chi-square test, as were the differences during the waiting period and during postoperative year separately. Kaplan-Meier method and log-rank test were used for a time-to-event analysis. We used the Kaplan-Meier method to estimate and compare the cumulative incidence of overall and cardiovascular-related mortality over the 1-year follow-up period. Sensitivity analyses of the primary outcome were conducted to assess the robustness of the findings, adjusting for baseline characteristics. Multivariable Cox regression analyses were performed for HRs and logistic regression analyses for ORs to evaluate the consistency of treatment effects. Because these sensitivity analyses were not specified in the statistical analysis plan, no prespecified selection of baseline variables

was made. Instead, the selection of baseline characteristics was determined ad hoc, based on recommendations by peer reviewers. These analyses were conducted for the whole study group and further stratified according to different procedure groups to examine potential variations across subgroups. Quality-of-life utility was compared between groups using the independent samples Student's *t*-test. Missing utility data were imputed using multiple imputation with m = 20, using predictive mean matching to draw imputed values. Further we performed an analysis of covariance to control for baseline measurements of quality of life. The effect of the teleprehabilitation program was assessed by comparing the incidence of the modifiable risk factors at baseline with the incidence at time of the index surgery (measured at hospital admission) within the intervention group, within the control group, and between groups. The effect of teleprehabilitation on modifiable risk factors between the intervention group and control group was analyzed using the Pearson chi-square test and independent Student's *t*-test, as appropriate. Differences between the 2 groups in length of hospital stay were tested using the independent samples Student's *t*-test. Differences in the occurrence of postoperative complications were tested using Pearson's chi-square test. The McNemar test was used to test whether the proportion of risk factors differs over time, stratified by intervention and control group. Pearson's chi-square test was used to test whether the 2 groups differ in the proportion of risk factors.

RESULTS

PATIENTS. From May 2020 to August 2022, a total of 394 patients were enrolled; 197 were assigned to the intervention group, and 197 to the control group (Figure 1). One patient in the control group withdrew informed consent. Overall, the groups were balanced with respect to baseline characteristics (Table 1). The median duration in weeks of the preoperative period was shorter in the intervention group (12.6 weeks [Q1-Q3: 7.5-19.4 weeks]) compared with the control group (14.8 weeks [Q1-Q3: 9.0-21.5 weeks]; $P = 0.024$). However, the number of patients who had a minimum prehabilitation duration of 8 weeks was not significantly different (see Supplemental Table 1). An overview of all procedures is presented in Supplemental Table 2, with the most commonly performed procedures being coronary artery bypass graft, minimally invasive direct coronary artery bypass, aortic valve replacement, TAVR, and aortic valve replacement + coronary artery bypass graft.

PRIMARY OUTCOME. The primary composite endpoint of MACE as measured from inclusion until 1 year after surgery, or end of follow-up, occurred in 16.8% (33 of 197) of the patients in the intervention group and in 25.5% (50 of 196) of the patients in the control group (difference 8.8%; 95% CI: 0.7-16.8; $P = 0.032$). The cumulative incidence of the primary composite endpoint and its subcategories is shown in Table 2.

The unadjusted OR for teleprehabilitation was 0.59 (95% CI: 0.36-0.97; $P = 0.037$), and the unadjusted HR was 0.62 (95% CI: 0.40-0.97; $P = 0.037$). To further analyze the impact of teleprehabilitation on the composite primary endpoint, we employed a multivariable Cox proportional hazards model. This model adjusted for the following covariates: intervention type, smoking status, left ventricular ejection fraction (LVEF) (as a continuous variable), and NYHA functional classification.

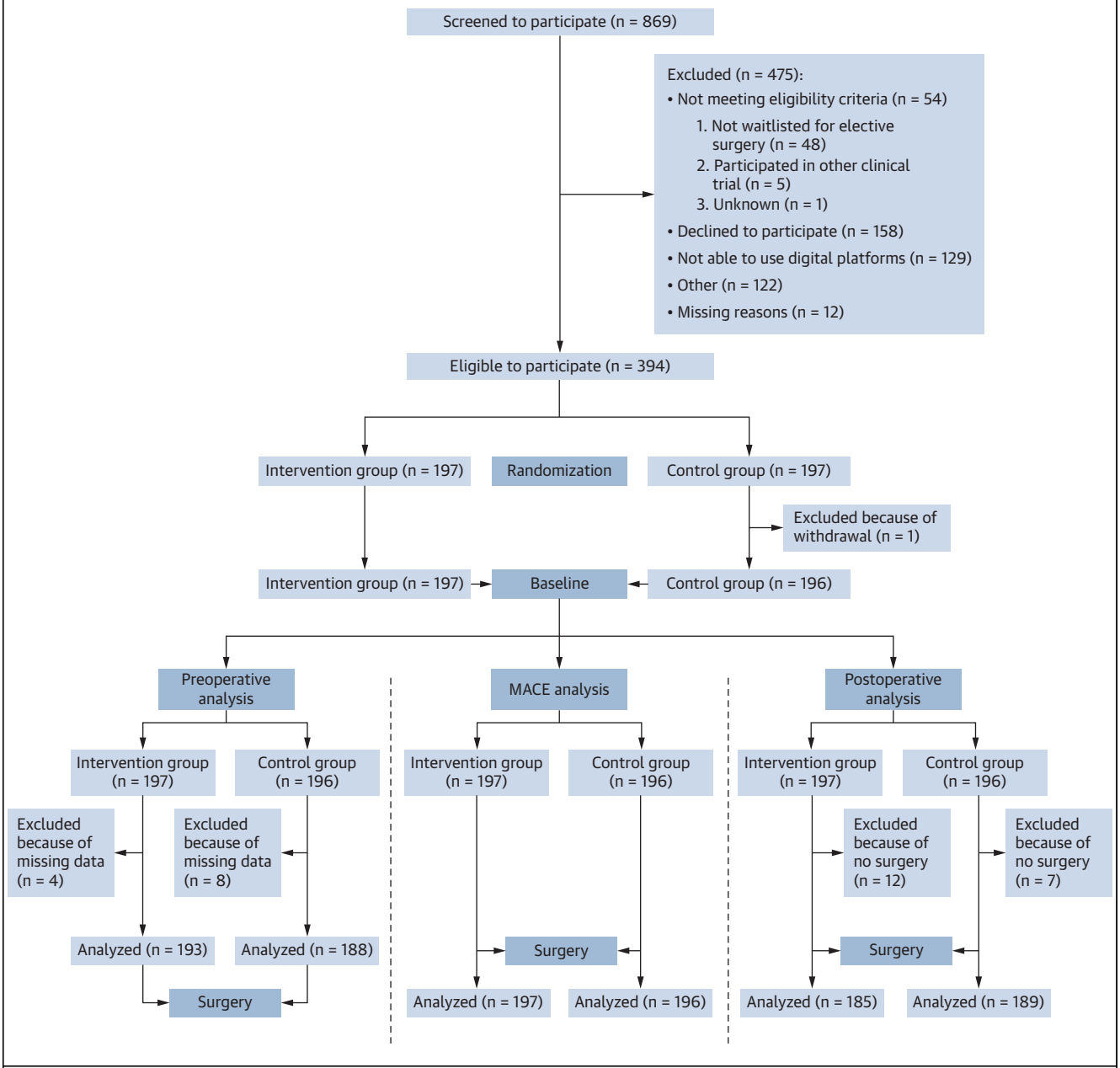
The adjusted HR for the entire cohort was 0.68 (95% CI: 0.44-1.06; $P = 0.089$). When stratified into 2 subgroups—transcatheter procedures combined with isolated atrial fibrillation (AF) ablation vs other procedures—the adjusted HR for the latter group was 0.59 (95% CI: 0.35-0.98; $P = 0.044$). In contrast, for the transcatheter procedures combined with isolated AF ablation subgroup, the adjusted HR was 1.05 (95% CI: 0.28-3.99; $P = 0.94$).

We also applied logistic regression analyses for adjusting the ORs to the same covariates. The adjusted OR for the entire cohort was 0.64 (95% CI: 0.39-1.06; $P = 0.086$). When stratified into 2 subgroups—transcatheter procedures combined with isolated AF ablation vs other procedures—the adjusted OR for the latter group was 0.54 (95% CI: 0.30-0.96; $P = 0.035$). In contrast, for the transcatheter procedures combined with isolated AF ablation subgroup, the adjusted OR was 1.05 (95% CI: 0.28-3.99; $P = 0.94$).

The treatment effect for the primary outcome in prespecified subgroups is shown in Figure 2. There was a significant effect in the subgroup of women (OR: 0.312; 95% CI: 0.109-0.895; $P = 0.030$), patients with a higher EuroSCORE II (OR: 0.492; 95% CI: 0.258-0.938; $P = 0.031$), and cardiac surgery group (OR: 0.49; 95% CI: 0.28-0.87; $P = 0.014$). The interaction *P* values for sex, sternotomy vs minimally invasive, EuroSCORE II, and cardiac surgery vs procedures were 0.174, 0.444, 0.843, and 0.547, respectively.

SECONDARY OUTCOMES. Quality of life at baseline, as measured with the EQ-5D-5L was 0.753 ± 0.196 in the intervention and 0.737 ± 0.231 in the control group. Quality of life 1 year after surgery, or at the end

FIGURE 1 **Flowchart of the Study Population**



MACE = major adverse cardiovascular events.

of follow-up, as measured with the EQ-5D-5L was 0.861 ± 0.143 in the intervention and 0.805 ± 0.198 in the control group (difference, 0.056; 95% CI: 0.020-0.092; $P = 0.002$). We evaluated the effect of prehabilitation on patients in both groups by comparing changes in quality of life from baseline to 12 months, using the EQ-5D scores (baseline vs 12 months). Complete data were available for 147 patients in the control group and 154 patients in the intervention group. Both groups showed improvements in quality of life, with the intervention group improving by 0.055 ± 0.255 ($P = 0.008$) and the control group improving by 0.044 ± 0.249 ($P = 0.033$). We also run an analysis of covariance to determine the effect of teleprehabilitation on the quality of life 1 year after surgery in comparison with the control group, after

TABLE 1 Baseline Characteristics

	Overall (N = 393)	Intervention Group (n = 197)	Control Group (n = 196)
Demographic characteristics			
Age, y	65.6 ± 9.2	65.6 ± 9.3	65.5 ± 9.2
Male	299 (76.1)	150 (76.1)	149 (76.0)
SES	−0.031 ± 0.213	−0.014 ± 0.206	−0.047 ± 0.218
Health-related characteristics			
BMI, kg/m^2	27.5 ± 4.5	27.4 ± 4.5	27.6 ± 4.6
COPD	33 (8.4)	16 (8.1)	17 (8.7)
Diabetes mellitus	75 (19.1)	36 (18.3)	39 (19.9)
Smoking status			
Current smoker	40 (10.2)	15 (7.6)	25 (12.8)
Former smoker	204 (51.9)	105 (53.3)	99 (50.5)
Never	149 (37.9)	77 (39.1)	72 (36.7)
EuroSCORE II	1.1 (0.75-1.72)	1.06 (0.71-1.70)	1.16 (0.77-1.73)
LVEF			
<50%	52 (13.2)	22 (11.2)	30 (15.3)
≥50%	341 (86.8)	175 (88.8)	166 (84.7)
eGFR, mL/min/1.73 m^2	88.1 ± 29.2	88.7 ± 29.1	87.6 ± 29.4
NYHA functional class			
I	89 (22.6)	49 (24.9)	40 (20.4)
II	172 (43.8)	86 (43.7)	86 (43.9)
III or IV	132 (33.6)	62 (31.4)	70 (35.7)
CCS class			
I	221 (56.2)	123 (62.4)	98 (50.0)
II	138 (35.1)	64 (32.5)	74 (37.8)
III or IV	34 (8.6)	10 (5.1)	24 (12.2)
Surgery characteristics			
Conventional (sternotomy)	216 (55.0)	108 (54.8)	108 (55.1)
Minimally invasive surgery (nonsternotomy)	177 (45.0)	89 (45.2)	88 (44.9)
Primary pathology			
Coronary disease	159 (40.5)	79 (40.1)	80 (40.8)
Coronary + valve disease	65 (16.6)	33 (16.7)	32 (16.4)
Coronary + ascending aortic aneurysm disease	4 (1.0)	1 (0.5)	3 (1.5)
Aortic valve stenosis	60 (15.3)	34 (17.3)	26 (13.3)
Aortic valve regurgitation	9 (2.3)	7 (3.6)	2 (1.0)
Mitral valve regurgitation	26 (6.6)	11 (5.6)	5 (2.6)
Tricuspid valve regurgitation	3 (0.8)	1 (0.5)	2 (1.0)
Multiple valve combined pathology (stenosis and regurgitation)	16 (4.1)	7 (3.6)	9 (4.6)
Ascending aortic aneurysm	7 (1.8)	2 (1.0)	5 (2.6)
Ascending aortic aneurysm + valvular pathology (stenosis and regurgitation)	19 (4.8)	7 (3.6)	12 (6.1)
Atrial fibrillation	16 (4.1)	11 (5.6)	5 (2.6)
Atrial fibrillation + valvular pathology (stenosis and regurgitation)	6 (1.5)	2 (1.0)	4 (2.0)
Other	3 (0.8)	2 (1.0)	1 (0.5)
Center			
MUMC+	104 (26.5)	50 (25.4)	54 (27.6)
Zuyderland	200 (50.9)	102 (51.8)	98 (50.0)
VieCuri	40 (10.2)	17 (8.6)	23 (11.7)
Laurentius	40 (10.2)	22 (11.2)	18 (9.2)
Other	9 (2.3)	6 (3.0)	3 (1.5)

Values are mean ± SD, n (%), or median (Q1-Q3).

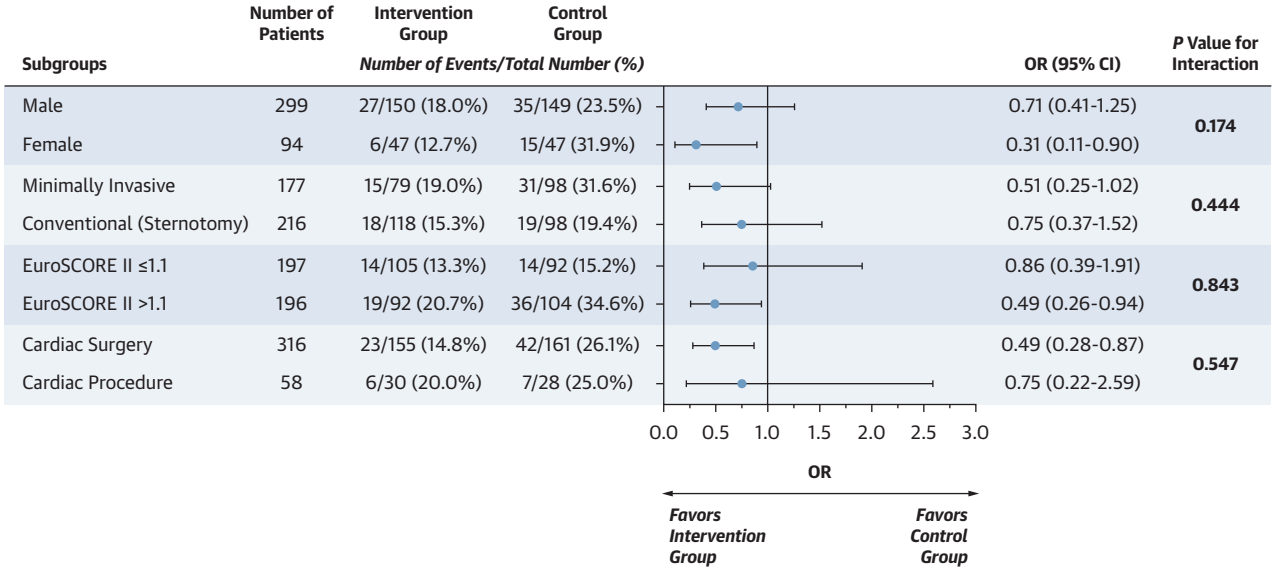
BMI = body mass index; CCS = Canadian Cardiovascular Society; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; HADS = hospital anxiety and depression scale; LVEF = left ventricular ejection fraction; MUMC+ = Maastricht University Medical Center; SES = socioeconomic status.

TABLE 2 Cumulative Incidence of the Primary Composite Endpoint and Subcategories, Postoperative Length of Hospital Stay, and Postoperative Complications

	Intervention Group (n = 197)	Control Group (n = 196)	*P* Value
Major adverse cardiovascular events	33 (16.8)	50 (25.5)	**0.032**
Cardiovascular death	10 (5.1)	4 (2.0)	0.105
Myocardial infarction	6 (3.0)	8 (4.1)	0.580
Stroke	2 (1.0)	8 (4.1)	0.062[a]
Hospitalization for heart failure or other life-threatening cardiac events	6 (3.0)	17 (8.7)	**0.019**
Earlier or repeated intervention	9 (4.6)	13 (6.6)	0.391
	Intervention Group (n = 185)	**Control Group (n = 189)**	***P* Value**
Postoperative length of hospital stay, d	6.3 ± 7.0	6.3 ± 7.0	0.915
Postoperative length of hospital stay in transcatheter and isolated atrial fibrillation procedures, d	5.6 ± 7.7	6.5 ± 11.3	0.725
Postoperative length of hospital stay in patients with cardiac surgery, d	6.4 ± 6.9	6.3 ± 6.4	0.919
Postoperative complications			
Any postoperative complication	55 (29.7)	73 (38.6)	0.070
Respiratory complication	10 (5.4)	9 (4.8)	0.777
Readmission ICU	5 (2.7)	6 (3.2)	0.787
Renal failure	5 (2.7)	4 (2.1)	0.749[a]
Cardiac arrhythmia	41 (22.2)	56 (29.6)	0.099
Sternal refixation	0 (0.0)	1 (0.5)	1.000[a]
Deep sternal wound infection	2 (1.1)	4 (2.1)	0.685[a]

Values are n (%) or mean ± SD. [a]Fisher exact test, 2-sided.
ICU = intensive care unit.

FIGURE 2 Forest Plot Showing ORs for Predefined Subgroups of the Incidence of the Primary Composite Endpoint of Major Adverse Cardiovascular Events

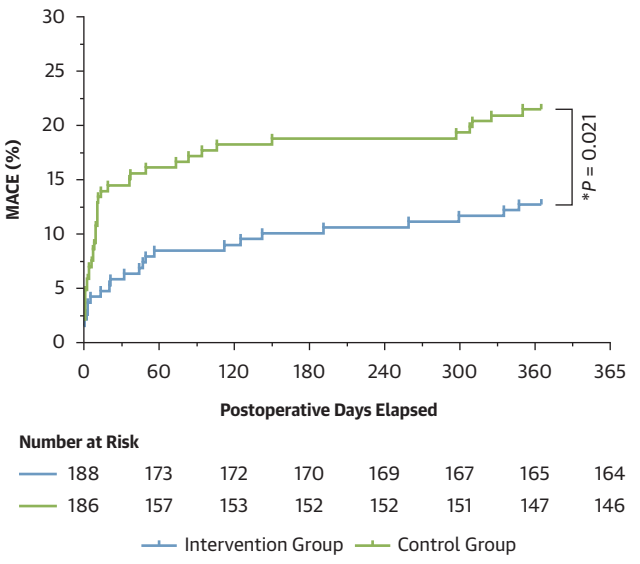


controlling for the quality of life at baseline. The quality of life was not statistically lower in the intervention group than in the control group (mean difference of 0.025 [95% CI: −0.017 to 0.068]; $P = 0.244$).

There was no significant difference in the occurrence of the MACE between the intervention group 4.6% (9 of 197) and the control group 5.1% (10 of 196) from inclusion to index surgery (preoperative period) ($P = 0.805$). However, a significant difference in the incidence of the MACE was observed after the index surgery (postoperative period), with rates of 12.8% (24 of 188) in the intervention group and 21.5% (40 of 186) in the control group ($P = 0.021$) (**Figure 3**). Additionally, there was no significant difference in the incidence of postoperative complications or length of hospital stay between the intervention and control groups (**Table 2**). We performed a sensitivity analysis on the length of hospital stay, stratifying the patients into 2 subgroups—transcatheter procedures or with isolated AF ablation vs other cardiac surgery procedures. For patients undergoing cardiac surgery procedures, the length of hospital stay was 6.3 ± 6.4 days in the control group compared with 6.4 ± 6.9 days in the teleprehabiltation group ($P = 0.919$). For patients with transcatheter procedures or with isolated AF ablation, the length of hospital stay was 6.5 ± 11.3 days in the control group compared with 5.6 ± 7.7 days in the teleprehabilitation group ($P = 0.725$).

There was no significant difference in all-cause mortality between the intervention group (n = 10) and the control group (n = 5) ($P = 0.192$), nor in cardiovascular mortality between the intervention group (n = 10) and the control group (n = 4) ($P = 0.107$) (Supplemental Figure 1). However, the mortality in the intervention group was higher. Of all participants who died, 2 died during the preoperative phase, 10 died during index surgery hospitalization from severe surgical complications, and only 3 patients died after hospital discharge. Of the 15 patients who died, 2 did not undergo any surgical treatment but were included as intention-to-treat analysis: one was because of a sudden cardiac arrest, and the other received a percutaneous coronary intervention because of progression of symptoms. The patient who received a percutaneous coronary intervention later died because of asystole in the preoperative phase. Both patients were part of the prehabilitation group. The causes of death in all 15 patients are depicted in Supplemental Table 3.

FIGURE 3 Time-to-Event Curve for the Incidence of MACE in the Postoperative Phase

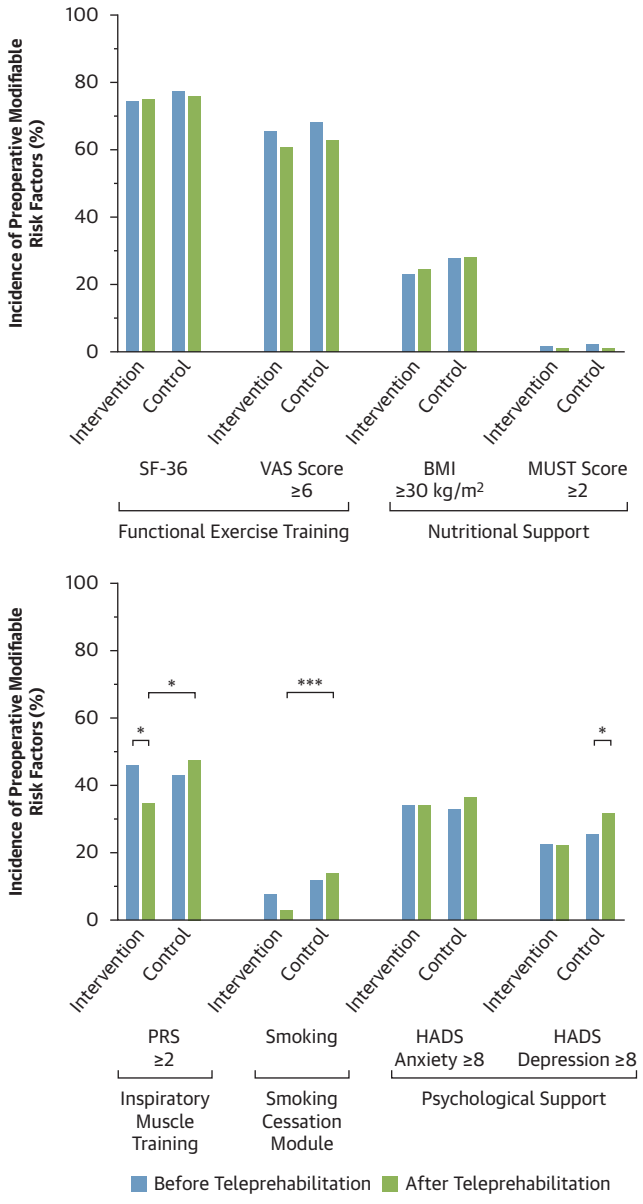


Major adverse cardiovascular events (MACE), with event rates of 12.8% (24 of 188) in the intervention group and 21.5% (40 of 186) in the control group ($P = 0.021$).

TELEPREHABILITATION PROGRAM. The incidence of preoperative modifiable risk factors in the total population was as follows: 87.4% of patients screened positive for functional exercise training, 45.1% had an elevated pulmonary risk score, and 43.6% had a positive HADS, with 34.4% of the population exhibiting a positive HADS-anxiety and 24.7% showing a positive HADS depression. Additionally, 27.9% had a positive screening for nutritional support, with 25.7% having a BMI ≥30 kg/m^2, and 2.4% presenting with a MUST score ≥2. Current smokers were observed in 10.2% of the population. On average, each patient had 2.1 modifiable risk factors at baseline.

In the intervention group, participation in prehabilitation modules was recorded only for patients who were eligible based on positive screening results. For functional exercise training, the participation rate was 66.3%, with a mean of 3.4 supervised consultations. Inspiratory muscle training had a participation rate of 48.3%, with patients attending an average of 3.9 consultations. For psychological support, the participation rate was 71.1%, with a mean of 2.5 consultations. Nutritional support had a participation rate of 24.5%, with patients attending 1.5 consultations on average. Smoking cessation had a

FIGURE 4 Incidence of Preoperative Modifiable Risk Factors in the Intervention and Control Group Before and After Teleprehabilitation



*$P < 0.050$. ***$P < 0.001$. BMI = body mass index; HADS = Hospital Anxiety and Depression Scale; MUST = Malnutrition Universal Screening Tool; PRS = pulmonary risk score; SF-36 = 36-item Short Form Health Survey; VAS = visual analogue scale.

participation rate of 60%, with a mean of 5.7 consultations. On average, patients in the intervention group participated in 1.2 prehabilitation modules.

The differences of the incidence of the modifiable risk factors in the intervention and control group at baseline and before the index surgery is shown in Figure 4. No differences were observed in preoperative physical fitness, incidence of obesity, or elevated MUST score. In the intervention group, a statistically significant decrease was observed in the incidence of an elevated pulmonary risk score, comparing baseline (46.1%) to the index surgery (34.7%) ($P = 0.027$), which was not observed in the control group. Moreover, a statistically significant difference in the incidence of an elevated pulmonary risk score was found at the time of the index surgery between the intervention (34.7%) and control group (47.6%) ($P = 0.041$). Additionally, there was a statistically significant difference in the incidence of active smokers between the teleprehabilitation and standard care groups at the index surgery (3.2% vs 14.2%; $P = 0.001$). In the control group, we observed a statistically significant increase in the incidence of a positive HADS-depression score from baseline (25.5%) to the index surgery (32.0%) ($P = 0.027$), which was not observed in the intervention group.

DISCUSSION

We found a clinically relevant and statistically significant effect of a personalized multimodal teleprehabilitation program on the incidence of MACE in patients undergoing elective cardiac surgery and procedures, comparing the intervention and control group. This reduction was primarily driven by a reduction in hospitalizations and the sensitivity analyses showed that treatment effect was mainly in the patients undergoing a cardiac surgery rather than transcatheter procedures. Another observation that underlines the clinically significant effect of teleprehabilitation is that the incidence of MACE was similar in both groups during the preoperative phase, and only became significantly different after surgery. This suggests that the teleprehabilitation program, aimed at reducing the incidence of adverse postoperative outcomes, did not lead to an increase in preoperative adverse events, and the significant effect, as intended, was on postoperative events.

Although our study population generally consisted of patients scheduled for elective surgery and procedures, reflecting a lower-risk cohort with a median EuroSCORE II of 1.1%, it also included individuals with more severe pathologies such as thoracic aneurysm, 3-vessel disease, and severe aortic valve stenosis; those with comorbidities like stroke, dialysis, and chronic obstructive pulmonary disease; the elderly; and those with higher surgery risks. Notably, patients requiring more urgent surgery, such as those with active endocarditis, acute aortic dissections, or

those clinically admitted following acute coronary syndromes, were not included in this trial. However, our previous investigation on nonparticipants in this trial showed that patients with higher-risk profiles—characterized by older age, lower SES, and higher EuroSCORE II—were less likely to participate,[15] which is consistent with previous research in cardiac (tele) rehabilitation.[21,22] This only underlines the significance of this trial because these patients with higher surgical risk profiles could potentially benefit even more from prehabilitation.

We found no significant difference in postoperative length of hospital stay or predefined postoperative complications, in contrast to some other research.[3,8] We postulate that length of hospital stay might be influenced by institutional factors, cultural practice differences, and patient preferences and therefore might not be a good measurement of the effect on (tele)prehabilitation.

Regarding patient-reported health-related quality of life, as measured by the EQ-5D-5L, results 1 year after surgery demonstrated a clinically relevant[23] and statistically significant improvement in favor of the intervention group. However, after controlling for quality of life at baseline, we found no statistically significant difference at 12 months. This finding is in line with other publications in cardiac prehabilitation showing mixed results, but none have included as extensive a follow-up period as our study.[6,7,24]

On average, patients presented with 2.1 modifiable risk factors at baseline, underscoring the importance of preoperative risk assessment and prehabilitation in this population. The prevalence of these risk factors was consistent with those observed in other cardiac surgery populations.[1,5,7,25,26] Over 70% of patients with a positive HADS score participated in the psychological support module, and 60% of current smokers were referred to the smoking cessation program. Participation in the nutritional support module was modest. Overall, the participation rate in the prehabilitation program was high compared with our previous experience with postoperative cardiac rehabilitation adherence. However, to the best of our knowledge, there is no directly comparable data. This elevated participation may be attributed to increased patient motivation for health behavior changes in the preoperative setting,[27-29] with this period potentially serving as a teachable moment.[30]

We did not observe an improvement in physical fitness during the teleprehabilitation program. Previous meta-analyses suggest that center-based functional exercise training can enhance preoperative walking distance in cardiac surgery patients.[2] Our home-based program, initiated during the COVID-19 pandemic, implemented low-intensity exercises to minimize adverse cardiac events, lacking direct supervision. COVID-19 restrictions also prevented baseline physical tests, which could have better identified patients who might benefit and improved program effectiveness. The absence of exercise testing limited our ability to tailor exercise intensity, potentially leading to undertraining and reduced effectiveness.

There was no statistically significant difference in mortality between the intervention and control group; however, there was a notable numeric difference in overall mortality. Mortality was analyzed on an intention-to-treat basis from inclusion up to 1 year postoperatively. Two patients in the intervention group died preoperatively: one sudden cardiac death in a 64-year-old patient with aortic aneurysm awaiting Bentall procedure, and the other a progressive heart failure in an 84-year-old patient with amyloidosis awaiting a TAVR procedure (2 deaths in the intervention group vs 0 in the control group). During the index surgery hospitalization, 10 patients died from surgical complications: 6 deaths in the intervention group and 4 in the control group. Postdischarge, 3 additional deaths occurred: 2 in the intervention group and 1 in the control group. After a detailed analysis of patient data and the timing of mortality events, we believe that the observed numeric difference, lacking statistical significance, is unlikely to be from chance.

STUDY LIMITATIONS. Global variation in clinical norms regarding the length of the preoperative period—and thus the available time for prehabilitation—can pose challenges to implementation across different countries. The multimodal nature of the program makes it challenging to discern which specific component contributed to the observed effects. Moreover, the effect of certain lifestyle interventions may differ between patient groups with different pathologies, such as atherosclerosis and mitral valve regurgitation. Additionally, there is potential for inclusion bias, because mainly patients with lower surgical risk were included, possibly underestimating the intervention's true effectiveness. Moreover, the limited sample size for certain secondary outcomes complicates definitive interpretation. Last, bias in event ascertainment cannot be ruled out because of the open-label trial design.

Our trial provides new evidence that teleprehabilitation reduces the incidence of MACE in

patients undergoing cardiac surgery, a finding not established in previous research. However, despite the benefits and common belief that preoperative optimization can improve postoperative outcomes in patients scheduled for cardiac surgery,[31] the lack of evidence, until now, on clinical endpoints of prehabilitation has hindered its implementation in routine clinical care,[32] and consequently, programs are not yet integrated into standard cardiac surgery care pathways nor recommended by established international guidelines. Our data suggest that prehabilitation is of value for patients undergoing cardiac surgery and should already be implemented as routine care in cardiac surgical pathways.

CONCLUSIONS

The current trial investigated the impact of a personalized multimodal teleprehabilitation program on the composite endpoint of MACE in patients undergoing elective cardiac surgery and procedures and showed that teleprehabilitation was effective in reducing the composite endpoint of MACE, primarily in patients undergoing cardiac surgery. Therefore, teleprehabilitation might be a valuable addition to the current postoperative rehabilitation programs for patients undergoing cardiac surgery.

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APPENDIX For expanded Methods and Results sections, trial protocol, statistical analysis plan, and supplemental tables and a figure, please see the online version of this paper.