BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-066435
Article Type:	Original research
Date Submitted by the Author:	07-Jul-2022
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Keywords:	REHABILITATION MEDICINE, Anxiety disorders < PSYCHIATRY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Impact of kinesiophobia on initiation of cardiac rehabilitation: a prospective cohort path analysis.

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Word count

Abstract: 249

Manuscript: 3024

References: 32

Keywords: kinesiophobia, fear of movement, cardiac rehabilitation, physical activity, path analysis, self-efficacy

Journal: BMJ Heart

ABSTRACT

Objectives: To identify factors associated with kinesiophobia (fear of movement) after cardiac hospitalization and to assess the impact of kinesiophobia on CR-initiation.

Methods: We performed a prospective cohort study in cardiac patients recruited at hospital discharge. We assessed kinesiophobia with the Tampa Scale for Kinesiophobia (TSK). For this study the total score was used (range 13-52). We assessed baseline factors (demographics, cardiac disease history, questionnaire data on anxiety, biopsychosocial complexity and self-efficacy) associated with kinesiophobia using linear regression (β) with backward elimination. Prospectively, the impact of kinesiophobia on probability of CR-initiation in the first 3 months after hospital discharge (subsample referred for CR) was assessed using logistic regression.

Results: In total, 149 patients (78.5% male) with a median (IQR) age of 65 (14) were included, of which 82 (59%) were referred for CR. Moderate and severe levels of kinesiophobia were found in 22.8%. In the total sample, kinesiophobia was associated with cardiac anxiety (β=0.33 95%CI: 0.19 to 0.48), social complexity (β=0.23 95%CI: 0.06 to 0.39) and higher education (β=-0.18 95%CI:-0.34 to -0.02). In those referred for CR, kinesiophobia was negatively associated with self-efficacy (β = -0.29 95% CI: -0.47 to -0.12) and positively with cardiac anxiety (β= 0.43 95%CI: 0.24 to 0.62). Kinesiophobia decreased the probability of CR-initiation (OR $^{Range13\text{-}52\ points}$ = 0.92 95%CI: 0.84 to 0.99).

Conclusion: In patients hospitalised for cardiovascular disease, kinesiophobia is associated with cardiac anxiety, social complexity, educational level and self-efficacy. Kinesiophobia decreased the likelihood of CR-initiation with 8% per point on the TSK.

IMPLICATIONS FOR PRACTICE

- **What is already known on this topic**

  Kinesiophobia is associated with decreased quality of life and reduced physical activity. Little is known about factors associated with kinesiophobia at hospital discharge and the impact of kinesiophobia on initiation of cardiac rehabilitation.

- **What this study adds**

  Mild (53.0%), moderate (22.1%) and severe (0.7%) levels of kinesiophobia at hospital discharge. Highly educated and self-efficacious patients had less kinesiophobia. Self-efficacious patients were more likely to initiate CR than non-self-efficacious patients. Kinesiophobia at discharge decreased the odds of CR-initiation by 8% per point increase on the Tampa Scale for Kinesiophobia in those referred for CR. The effect of cardiac anxiety on uptake of CR was partly mediated by kinesiophobia.

- **How this study might affect research, practice or policy**

  Kinesiophobia at hospital discharge is associated with social and psychological factors. Tailoring phase 1 cardiac rehabilitation to the characteristics of patients with high levels of kinesiophobia might improve initiation of phase 2 cardiac rehabilitation.

INTRODUCTION

Fear of movement (kinesiophobia) is present in 45% of patients with cardiovascular disease (CVD) at the start of cardiac rehabilitation (CR) and remains present in 20% of patients after 3-10 months after hospital discharge. Kinesiophobia is associated with decreased quality of life and low PA-levels [1][2][3]. Moreover, kinesiophobia negatively impacts the uptake of cardiac rehabilitation (CR), despite CR's proven benefits such as reduced morbidity and mortality, and better psychological wellbeing [4][5][6].

The effect of kinesiophobia at hospital discharge on the uptake of CR has not been prospectively investigated. Previous qualitative research has shown that patients attribute high levels of kinesiophobia to a lack of support and information at hospital discharge from a health care provider [3]. Insight in factors associated with kinesiophobia at hospital discharge, and how kinesiophobia impacts CR-initiation, could help to identify potential determinants of kinesiophobia, which in turn could potentially impact CR-initiation, and help to adequately support and refer those with kinesiophobia.

Therefore the aims of this study were to explore (1) factors associated with kinesiophobia at hospital discharge and (2) the impact of kinesiophobia on initiation of cardiac rehabilitation.

METHODS

Study design

We performed a prospective cohort study from in patients hospitalised with cardiovascular disease from hospital discharge up to 3 months follow-up. To explore factors associated with kinesiophobia and the effect of kinesiophobia on CR-initiation, a hypothetical path-model was developed (explained in detail below) **(Figure 1).** Patients were included at hospital discharge (or shortly after) from the Amsterdam University Medical Centre at the department of Cardiology.

fig1:hypotheticalpathmodel

Ethics consideration

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Patient population

Eligible patients had been hospitalized for acute coronary syndrome (ACS), stable angina pectoris (AP), acute heart failure (AHF) or atrial fibrillation (AF). Exclusion criteria were: referral to a nursing home; inability to complete questionnaires, e.g. due to language problems.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Sample size considerations

Based on previous research we expected to include 10 variables in our final path-model [2]. We therefore aimed to include 15 times the number of parameters in our study, resulting in a final sample size of 150 patients [7].

Data collection and measurements

Patients were identified between August 2019 and May 2021 through the electronic health records system of the Amsterdam University Medical Centers. During hospitalisation, eligible patients were approached by study personnel of the Amsterdam University of Applied Sciences and, if they consented, enrolled in this study. The following data were collected from the electronic health record: age, sex, educational level, marital status, cardiac diagnosis and disease history. Patients were asked by email to complete questionnaires about their biopsychosocial complexity, the level of self-efficacy, anxiety and depression at discharge.

Outcomes

The primary outcomes were kinesiophobia at hospital discharge and CR-initiation (yes/no) 3 months after discharge. At hospital discharge, patients completed the Tampa Scale for Kinesiophobia (TSK-NL Heart). The TSK-NL Heart consists of 13 questions with a four-point scale ranging from 1 to 4, with a minimum score of 13 and maximum score of 52 points. Scores on the TSK-NL Heart are categorized as follows: subclinical: 13–22; mild: 23–32; moderate: 33–42; and severe: 43–52 [1]. After 3 months patients were asked, by telephone, if they 1) were referred for CR, 2) initated CR 3) were readmitted to the hospital for an unplanned procedure.

Self-reported measurements

All self-reported measurements were completed during, or shortly after, hospital discharge (maximum 2 days).

Biopsychosocial complexity

Patients' biopsychosocial complexity was assessed with the Intermed Self-Assessment (IMSA). The IMSA has four domains: biological complexity (chronicity and severity of symptoms, complications and life threat), psychological complexity (restrictions in coping, resistance to treatment, mental health threat, psychiatric dysfunction) and social complexity

(social dysfunction, residential instability). Scores >19 indicate high complexity. In this study, the biological, psychological and social domains were analysed separately [8].

Generic anxiety and depression

Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS). A sum score of 8-10 is defined as `possible anxiety/depressive disorder', a sum score of 11-21 is defined as `likely anxiety/depression disorder' [9].

Cardiac anxiety

The cardiac anxiety questionnaire (CAQ) is an 18-item, self-report questionnaire, designed to measure cardiac anxiety (fear, attention, avoidance of physical exercise and safety-seeking behaviour), rated on a 5-point Likert scale ranging from 0 (never) to 4 (always) [10].

Self-efficacy

Self-efficacy was assessed with the General Self-Efficacy Scale (GSES). The GSES is a 10 item questionnaire with a four-point Likert scale ranging from 0 (completely disagree) to 4 (completely agree). A higher sum score indicates better self-efficacy [11].

Statistical analysis

Descriptive statistics

Patient characteristics are presented as median and interquartile range (IQR) or numbers (%). We analysed baseline kinesiophobia and differences between patients based on CR-referral and CR- initiation. In addition, we assessed which patients were readmitted to the hospital for acute coronary syndrome, revascularization or electro-cardioversion within the period of this study (3 months).

Path analysis

We explored direct effects (relations between independent and dependent variables) and indirect effects (the effect of an independent variable on a dependent variable through one or more intervening or mediating variables) [12] **(Figure 1).** Since little is known about

kinesiophobia in patients with CVD, a comprehensive approach was used to explore the association between baseline variables, kinesiophobia and the initation of CR. We studied the association between demographic variables (age, sex, educational level), medical variables (diagnosis, cardiac disease history, risk factors), psychological variables (biopsychosocial complexity, generic anxiety, cardiac anxiety, self-efficacy) and kinesiophobia. Categorical variables were recoded into dummy variables (educational level, diagnosis, cardiac disease history, risk factors). All other variables (age, BMI, kinesiophobia, psychological variables). were analysed as continuous. In addition, we studied the longitudinal association between kinesiohobia, the abovementioned demographic, medical, psychological variables and CR-initiation. An overview of all analyses is found in online **appendix 1, table 1.**

First, univariable linear regression was used to select variables associated with kinesiophobia (TSK-NL Heart total score). Univariable logistic regression was used to select variables associated with CR-initiation in a subsample that was referred for CR (cut-off for variable retainment in both analyses: P<0.10) [13]. Second, a path analysis was conducted. Backward elimination was used to select significant (P<0.05) variables associated with kinesiophobia. The initiation of CR (yes/no) was regressed on kinesiophobia to study the direct effect of kinesiophobia on CR-initiation and possible indirect effects of baseline variables on CR-initiation, with kinesiophobia as mediator. Path analyses were conducted for the total sample and in a subsample that was referred for CR.

All effects on kinesiophobia (continuous TSK-NL Heart score) are presented as standardized beta estimates (β). Effect size of (β) was interpreted as small (<0.29), moderate (0.30 - 0.49), large (> 0.50) [14]. Effects on the uptake of CR are presented as odds ratios. In the final model, the effect of kinesiophobia on CR-initiation was corrected for age and gender. The Satorra-Bentler scaled chi square test (X^2) was used to assess model fit. Patterns of missing data were analysed with Little's test to assess the pattern of missing data. A full conditional specification Multiple Imputation (FCS MI) [15]. Data-imputation was

conducted in SPSS V28. An overview of all missing data is found in **Online Appendix 1, Table 1.** All descriptive and univariable analyses were performed in SPSS V28. The path models were analysed using Mplus V8.0.

RESULTS

Demographic and clinical characteristics

In total, 188 patients were assessed for eligibility. After inclusion, 39 patients (20.7%) did not complete any questionnaires, and 2 died. At hospital discharge, 82 (55%) patients were referred for CR, of which 61 (40.9%) initiated CR in 3 months follow up **(figure 2).**

fig2:flowchartstudy

Finally, 149 patients were included in the analyses with a median age of 65 years (range 32-86). The majority of patients were male (78.5%) and lived with a partner (77.9%). Most patients had been admitted for an elective intervention (55.7%), of which 78.5% underwent a PCI. A history of hypertension was present in 40.9%, dyslipidaemia in 26.2% and diabetes mellitus in 17.4. Prior myocardial infarction was present in 23.4% and prior PCI in 37.6% **(table 1).** The distribution of kinesiophobia levels were: subclinical (24.2%), mild (53.0%), moderate (22.1%) and severe (0.7%) **(figure 3).**

At baseline, TSK-scores were, on average, 3 points higher in patients who were referred but and did not initiate CR, than in those who did initiate CR (30.39 ± SD 6.76 vs 27.37 ± SD 5.98). Within 3 months follow up, 15 patients (10%) were readmitted to the hospital: 6 patients for ECV, 6 patients for PCI, 2 patients for ACS and 1 patient for acute heart failure.

fig3:kinesiophobiascores

Table 1: Baseline characteristics

(N=149)	
Demographics	
Age, years, mean (SD)	65.5 (14)
Male (%)	117 (78.5)
Higher education (%)	39 (26.2)
Lives with partner (%)	116 (77.9)
Index event (%)	
Acute Coronary Syndrome	
STEMI	32 (21.5)
NSTEMI	22(14.8)
UAP	9 (6.0)
Stable Angina revascularization	58 (38.9)
Acute Heart Failure	3 (2.0)
Atrial Fibrillation	25 (16.7)
Admission type (%)	
Acute admission	66 (44.3)
Elective admission	83 (55.7)
Treatment for index event (%)	
PCI	117 (78.5)
ECV	24 (16.1)
Medication only	8 (5.4)
Cardiac disease history (%)	
Myocardial infarction	35 (23.4)
PCI	56 (37.6)
CABG	5 (3.4)
Stroke	14 (9.4)
Peripheral artery disease	10 (6.7)
Cardiovascular disease risk factors [b] (%)	
Diabetes Mellitus type 2	26 (17.4)
History of hypertension	61 (40.9)
History of dyslipidaemia	39 (26.2)
BMI category (kg/m^2)	
18- 25	16 (10.8)
25-30	120 (80.5)
>30	13 (8.7)

[a] Multiple diagnoses possible
Values presented as median (IQR) and counts (%)
STEMI: ST-Elevation Myocardial Infarction,
NSTEMI: Non ST-Elevation Myocardial Infarction,
UAP: Unstable Angina Pectoris,
PCI: Percutaneous Coronary Intervention,
ECV: Electro Cardio Version,
CABG: Coronary Artery Bypass Grafting,
BMI: Body Mass Index.

Univariable analyses

An overview of all our univariable linear regression analyses is presented in **table 2.** We found small associations between kinesiophobia and female sex (β= 0.19 95% CI: 0.03 to 0.35) , Age ≤ 50 (β = 0.22 95% CI: 0.38 to 2.49), (HADS anxiety (β = 0.27 95% CI: 0.11 to 0.42). Higher education (β=-0.24 95% CI: -0.40 to -0.08) and GSES self-efficacy (β=-0.18 95% CI: -0.34 to -0.02) were negatively associated with kinesiophobia. Moderate associations were found between kinesiophobia and HADS Depression (β=0.32 95% CI:0.16 to 0.47), IMSA psychological complexity (β = 0.32 95% CI: 0.17 to 0.48), IMSA social complexity (β=0.33 95% CI: 0.17 to 0.48) and CAQ cardiac anxiety (β=0.42 95% CI: 0.27 to 0.57).

Table 2: Univariable Linear regression with TSK-NL Heart as dependent variable (N=149)

Variable	Standardized Beta (95% CI)	Adjusted R-square	P-value
Demographics			
Age (continuous)	-0.13 (-0.29 to 0.04)	0.001	0.13
Age ≤ 50	0.22 (0.38 to 2.49)	0.05	0.008
Female Sex	0.19 (0.03 to 0.35)	0.03	0.02
Higher Education	-0.24 (-0.40 to -0.08)	0.05	0.003
Index event			
Acute coronary syndrome	0.08 (-0.08 to 0.25)	0.001	0.31
Stable angina revascularization	-0.04 (-0.21 to 0.12)	-0.001	0.61
Atrial Fibrillation	-0.04 (-0.21 to 0.12)	-0.001	0.59
Admission			
Acute admission	0.07 (-0.09 to 0.24)	0.001	0.37
Treatment index event			
PCI	0.02 (-0.14 to 0.19)	-0.01	0.79
ECV	-0.02 (-0.19 to 0.14)	-0.01	0.99
Medication only	-0.01 (-0.16 to 0.16)	-0.01	0.99
Cardiac disease history			
Acute coronary syndrome	-0.08 (-0.25 to 0.08)	0.001	0.32
PCI	0.001 (-0.16 to 0.16)	-0.001	0.49
CABG	0.06 (-0.10 to 0.22)	-0.001	0.46
Stroke	-0.11 (-0.28 to 0.49)	0.001	0.17
Peripheral artery disease	0.03 (-0.13 to 0.20)	-0.001	0.40
CVD risk factors			
Diabetes mellitus	-0.02 (-0.18 to 0.15)	-0.001	0.83
History of hypertension	0.03 (-0.13 to 0.20)	-0.01	0.69
History of dyslipidaemia	0.08 (-0.09 to 0.24)	-0.001	0.35
BMI	0.14 (-0.19 to 0.30)	0.01	0.08
Psychological risk factors			
GSES General Self-Efficacy scale	-0.18 (-0.34 to -0.02)	0.03	0.03
HADS Anxiety	0.27 (0.11 to 0.42)	0.06	0.001
HADS Depression	0.32 (0.16 to 0.47)	0.09	0.001
IMSA Biological complexity	0.21 (0.06 to 0.37)	0.04	0.009
IMSA Psychological complexity	0.32 (0.17 to 0.48)	0.10	0.001
IMSA Social complexity	0.33 (0.17 to 0.48)	0.10	0.001
CAQ Cardiac anxiety	0.42 (0.27 to 0.57)	0.17	0.001

GSES: General Self Efficacy Scale, HADS: Hospital Anxiety and Depression Scale, IMSA: InterMed Self-Assessment, CAQ: Cardiac Anxiety Questionnaire

In patients referred for CR (N=82), 9 candidate predictors of CR-initiation were found. TSK Kinesiophobia (OR: 0.92 95% CI: 0.85 to 1.00), treatment with ECV (OR:0.21 95% CI: 0.07 to 0.69), atrial fibrillation (OR: 0.21 95% CI: 0.07 to 0.69), HADS anxiety (OR: 0.89 95% CI: 0.79 to 1.00), HADS depression (OR:0.93 95%CI: 0.81 to 1.06), and IMSA psychological complexity (OR: 0.82 95% CI: 0.66 to 1.00) decreased the odds of CR initiation. Treatment with PCI (OR: 3.56 95% CI: 1.15 to 11:00), acute admission (OR: 2.58 95% CI: 0.89 to 7.54) and GSES Self-efficacy (OR: 1.18 95% CI: 1.03 to 1.36) increased the odds for CR initiation **(table 3).** In those referred for CR, 7 patients were readmitted to the hospital for an unplanned procedure, of which 6 initiated CR (OR: 2.18 95%CI: 0.32 to 2.85). An overview of all candidate predictors of CR in the total sample (N=149) is found in **Online Appendix 2 Table 2.**

Table 3: Univariable logistic regression with CR initiation as dependent variable in a subsample referred for CR (N=82)

Variable	CR-initiation No (N=21)	CR-initiation Yes (N=61)	OR (95% CI)	P-value
Demographics				
Age	63 (11.0)	63 (19.0)	0.98 (0.94 to 1.01)	0.49
Age ≤ 50	1 (1.2)	12 (14.6)	4.90 (0.60 to 40.22)	0.14
Age >50	20 (24.4)	49 (59.8)	0.20 (0.03 to 1.66)	0.14
Female sex (%)	7 (33.3)	11 (18.0)	0.44 (0.14 to 1.36)	0.14
Higher education (%)	16 (23.9)	19 (31.1)	1.92 (0.57 to 6.46)	0.29
Index event				
Acute coronary syndrome (%)	6 (28.6)	30 (49.2)	2.42 (0.83 to 7.11)	0.11
Stable angina revascularization (%)	7 (33.3)	23 (37.7)	1.21 (0.43 to 3.44)	0.72
Atrial fibrillation (%)	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.68)	0.01
Admission type				
Acute admission index event	6 (4.0)	31 (20.8)	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	1 (4.8)	6 (9.8)	2.18 (0.25 to 19.22)	0.48
Treatment index event				
PCI	13 (61.9)	52 (85.2)	3.56 (1.49 to 16.00)	0.03
ECV	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.69)	0.10
Medication only	-	2 (3.3)	-	-
Cardiac disease history				
Acute coronary syndrome	3 (14.3)	15 (24.6)	1.96 (0.51 to 7.58)	0.33
PCI	9 (42.9)	22 (36.1)	0.75 (0.27 to 2.07)	0.58
CABG	-	4 (6.6)	-	-
Stroke	2 (9.5)	2 (3.3)	0.33 (0.42 to 2.45)	0.27
Peripheral artery disease	1 (4.8)	2 (3.3)	0.68 (0.06 to 7.38)	0.76
CVD risk factors				
Diabetes Mellitus (%)	4 (19.0)	11 (18.0)	0.94 (0.26 to 3.33)	0.92
Hypertension (%)	8 (38.1)	23 (37.7)	0.98 (0.35 to 2.73)	0.98
Dyslipidemia (%)	5 (23.8)	19 (31.1)	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.07 (1.16)	27.02 (1.20)	0.96 (0.78 to 1.18)	0.69
Psychological risk factors				
Median TSK Kinesiophobia (IQR)	29.00 (10.78)	27.93 (7.00)	0.92 (0.85 to 1.00)	0.06
Median GSES Self-Efficacy (IQR)	32.67 (5.50)	33.49(7.00)	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	7.00 (4.00)	5.39(4.99)	0.89 (0.79 to1.00)	0.06
Median HADS Depression (IQR)	5.00 (5.21)	4.00(5.70)	0.93 (0.81 to1.06)	0.06
Median IMSA Biological complexity	14 (2.63)	15 (4.00)	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.64(4.0)	5.42(2.81)	0.82 (0.66 to1.00)	0.06
Median IMSA Social complexity (IQR)	7.89 (3.50)	8.64 (3.00)	1.02 (0.83 to 1.27)	0.84
Median CAQ Cardiac Anxiety	26.45 (7.00)	27.00 (11.00)	0.97 (0.92 to 1.03)	0.36

Path analysis

Analysis 1: Total sample

In the total sample we identified three variables that were associated with kinesiophobia **(table 4).** CAQ cardiac anxiety (β = 0.33 95% CI: 0.19 to 0.48) was moderately associated with kinesiophobia. A small association was found between kinesiophobia and IMSA social complexity (β = 0.23 95% CI: 0.06 to 0.39) and higher education (β = -0.18 95% CI: -0.34 to -0.02). We identified two predictors of CR-initiation: age (years) (OR: 0.96 95% CI: 0.93 to 0.99) decreased, while higher levels of GSES self-efficacy (OR: 1.10 95% CI: 1.01 to 1.20) increased the odds for CR-initiation. An overview of all variables associated with kinesiophobia and CR-initiation are presented in a path analysis diagram **(figure 4).**

Model fit (X^2= -2.254124, DF:0.972, P = 1.00).

fig4:pathmodeltotal

Table 4: Path analysis with TSK and CR as dependent variables (N=149)

Dependent variable: TSK		
Variable	**Standardized Beta (95% CI)**	**P-value**
CAQ Cardiac anxiety	0.33 (0.19 to 0.48)	0.001
IMSA Social complexity	0.23 (0.06 to 0.39)	0.006
Higher Education	-0.18 (-0.34 to -0.02)	0.03
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
Age	0.96 (0.93 to 0.99)	0.02
GSES Self-Efficacy	1.10 (1.01 to 1.20)	0.03

Analysis 2: Subsample referred for CR

In the subsample that was referred for CR, we identified two variables that were associated with kinesiophobia **(table 5).** A moderate positive association was found between CAQ cardiac anxiety (β = 0.43 95% CI: 0.24 to 0.62) and kinesiophobia, while GSES self-efficacy (β=-0.29 95% CI: -0.47 to -0.12) was negatively associated with kinesiophobia. Age (OR= 0.98 95% CI: 0.94 to 1.02) was kept in the model since model fit decreased after omission of this variable and age <50 was significantly associated with kinesiophobia and initiation of CR **(table 2)** and **(online appendix 2).** Corrected for age, kinesiophobia (OR=0.92 95% CI: 0.84 to 0.99) significantly decreased the odds of CR-initiation. A moderate indirect effect of CAQ cardiac anxiety (OR = 0.98 95% CI: 0.95 to 1.00) on CR-initiation was found with kinesiophobia as a mediator. The subsample analysis is presented in a path analysis diagram **(figure 5).** Model fit (X^2= -0.0062, DF: 0.973, P = 1.00).

fig5:pathmodelsubsample

Table 5: Path analysis with TSK and CR- initiation as dependent variables, restricted to patients who had been referred to CR (N=82)

Dependent variable: TSK		
Variable	**Standardized Beta (95%CI)**	**P-value**
CAQ Cardiac anxiety	0.43 (0.24 to 0.62)	0.001
GSES Self-Efficacy	-0.29 (-0.47 to -0.12)	0.001
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
TSK Kinesiophobia		
Model a	0.92 (0.85 to 0.99)	0.05
Model b	0.92 (0.84 to 0.99)	0.04
Model c	0.93 (0.86 to 1.01)	0.08
Model c+d	0.92 (0.85 to 1.01)	0.07
Mediation analysis: indirect effect of cardiac anxiety an self-efficacy on CR-initiation with TSK as mediator		
Variable	**OR (95%CI)**	**P-value**
CAQ Cardiac Anxiety	0.98 (0.95 to 1.00)	0.05
GSES Self-efficacy	1.04 (0.99 to 1.09)	0.11

a = Crude association b = Corrected for age, c = Corrected for gender, d = Corrected for age + gender

DISCUSSION

We found that mild and moderate levels of kinesiophobia were present at hospital discharge in a substantial group of patients with CVD (53% and 22.1% respectively). Cardiac anxiety, social complexity, and educational level were associated with kinesiophobia at hospital discharge. In patients who were referred for CR, self-efficacy was negatively associated with kinesiophobia. In patients referred for CR, the presence of kinesiophobia was associated with a lower rate of CR initiation. An indirect effect of cardiac anxiety on CR-initiation was found.

Our study shows that kinesiophobia decreases the likelihood of CR initiation. Theoretically this makes sense since the construct kinesiophobia comprises `fear of injury', `perception of risk' and `avoidance of physical activity'. Patients with higher levels of kinesiophobia might associate participation in CR as threatening since exercise and physical activity are the cornerstones of CR.

We identified a moderate association between cardiac anxiety and kinesiophobia. In a previous study a similar result was found [1]. Moreover, we found that kinesiophobia mediated the relationship between cardiac anxiety and CR-initiation. This finding is in line with previous research which reports that kinesiophobia mediates the relationship between self-rated anxiety and CR-attendance [4]. The CAQ measures behaviour and anxiety-related symptoms (e.g. *"I avoid activities that make my heart beat faster"*) whereas the TSK-NL Heart measures patients' beliefs about their physical state (e.g. *"If I tried to be physically active my heart problem would increase"*). More research is needed to investigate the impact of specific kinesiophobic beliefs on behaviour and anxiety related symptoms and vice versa.

In line with our findings, Brunetti et al, showed that educational level was negatively associated with kinesiophobia [16]. In a previous study, we found that patients with high levels of kinesiophobia often do not understand medical information and misinterpret body signals, which in turn is associated with poor health literacy and low educational level [3][17].

This finding fits well with the call for more tailored and understandable information at hospital discharge, provided by a trained healthcare provider [3].

Patients scoring high on social complexity suffered from higher levels of kinesiophobia. This is in line with our previous study where we found that patients with lower levels of kinesiophobia often experienced greater social support than those with higher levels of kinesiophobia [3]. The presence of a partner has been shown to improve lifestyle modification in cardiac patients and increase adherence to CR [18]. Moreover, participation of partners in CR-programs improves PA-levels in patients [19][20]. Future studies should evaluate the role of social support on levels of kinesiophobia after cardiac hospitalization.

Self-efficacy was negatively associated with kinesiophobia, in those referred for CR, and predicted CR-initiation in the total sample. Self-efficacy refers to `one's belief in their capacity to execute behaviours necessary to produce specific performance attainments' [21]. The association between self-efficacy and kinesiophobia has been established in patients with musculoskeletal disorders, but not in patients with CVD [22][23]. Zelle et al., reported that the impact of kinesiophobia on physical activity is largely mediated by self-efficacy, and should therefore be evaluated when targeting kinesiophobia [24]. Our study showed that self-efficacy increased the likelihood of CR-initiation by 10%. Self-efficacy is linked to CR-initiation, but is often lacking in patients with psychological distress [25]. Therefore, self-efficacy-building activities should be considered *before* CR-initiation [26]. Currently, behaviour change strategies are offered in CR-programs to improve PA levels, promote smoking cessation and a healthy diet [27]. However, these interventions are currently limited to those that initiate CR. An early behavioural intervention, aimed at reducing kinesiophobia and stimulating self-efficacy shorty after hospital discharge might improve CR-initiation.

Strengths and limitations

There are several strengths to our study. First, we studied kinesiophobia and CR-initiation using a prospective design. We were therefore able to study the temporal sequence of

kinesiophobia and CR-initiation, and multiple effects that impacted our outcomes. Second, using a path model allows for the specification of multiple, dependent and independent variables simultaneously and thereby gives insight into complex relationships between variables [12]. Our comprehensive path analysis gives insight in the factors that are associated with kinesiophobia and predict CR-initiation. These findings aid the development of tailored interventions to target kinesiophobia and improve CR-initiation.

We see the following limitations to this study. First, a substantial number of patients were included after the start of the COVID-19 pandemic. Although CR was offered remotely, this might have impacted kinesiophobia levels and CR-initiation. Second, by using path analysis we were able to explore a network of sequential relations with contributions from all paths (direct and indirect). Conceptually, a mediation model (in contrast to a confounding model) assumes that a series of variables relate via a causal chain of effect and each variable in the model affects variables occurring later in the chain [28]. In our model, an indirect effect of cardiac anxiety, through kinesiophobia, was found on CR-initiation. Theoretically, our finding makes sense, since somatic symptoms such as chest pain or palpitations (cardiac anxiety), can lead to negative beliefs about one's physical state (kinesiophobia), which in turn might lead to not initiating CR. Future studies should evaluate the potential mediating role of kinesiophobia in the uptake of CR. Third, although our interest is in causes of kinesiophobia and kinesiophobia as a cause of CR-initiation, our observational study does not permit any claims with regard to causal inference since necessary conditions for causal inference (exchangeability, positivity and consistency) have most likely not been met [29]. Nevertheless, this study reports important associations between baseline variables and kinesiophobia. In addition, we showed that kinesiophobia decreased the likelihood of CR-initiation. Future studies, using a causal design can use these results to investigate determinants of kinesiophobia and the effect of kinesiophobia on CR-initiation.

CONCLUSION

Kinesiophobia is prevalent at hospital discharge. Path analysis revealed that cardiac anxiety and social complexity were positively associated, whereas educational level, and self-efficacy were negatively associated with kinesiophobia at hospital discharge. In addition, patients with (high levels of) kinesiophobia were less likely to initiate cardiac rehabilitation.

Acknowledgement:

The authors are grateful to department of Cardiology of the Amsterdam University Medical Centre, all research nurses involved in the data collection and patients who participated in this study: Hiltje van der Werf, Manon Ootes, Marjon van Maarl and Willeke Veenhuizen.

Contributors:

GR, BV, HTJ, CHM and WSoR participated in the design of the study. PK and ICDvD were responsible for coordination and acquisition of the data. PK, KK and GR performed the statistical analysis. All authors contributed to the preparation, critical review and pproved the final manuscript.

Funding:

Financial support was received from the Dutch Research Council (NWO) as a personal grant (PK; nr: 023.010.064) and a RAAK-PRO grant (RAAK.PRO02.083).

The funding bodies had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Data availability statement

Data are available on reasonable request. Requests for analyses of data from this study should be directed to: P Keessen (p.keessen@hva.nl).

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Conflict of interest

We have read and understood BMJ policy on declaration of interests and declare that we have no conflicting interests.

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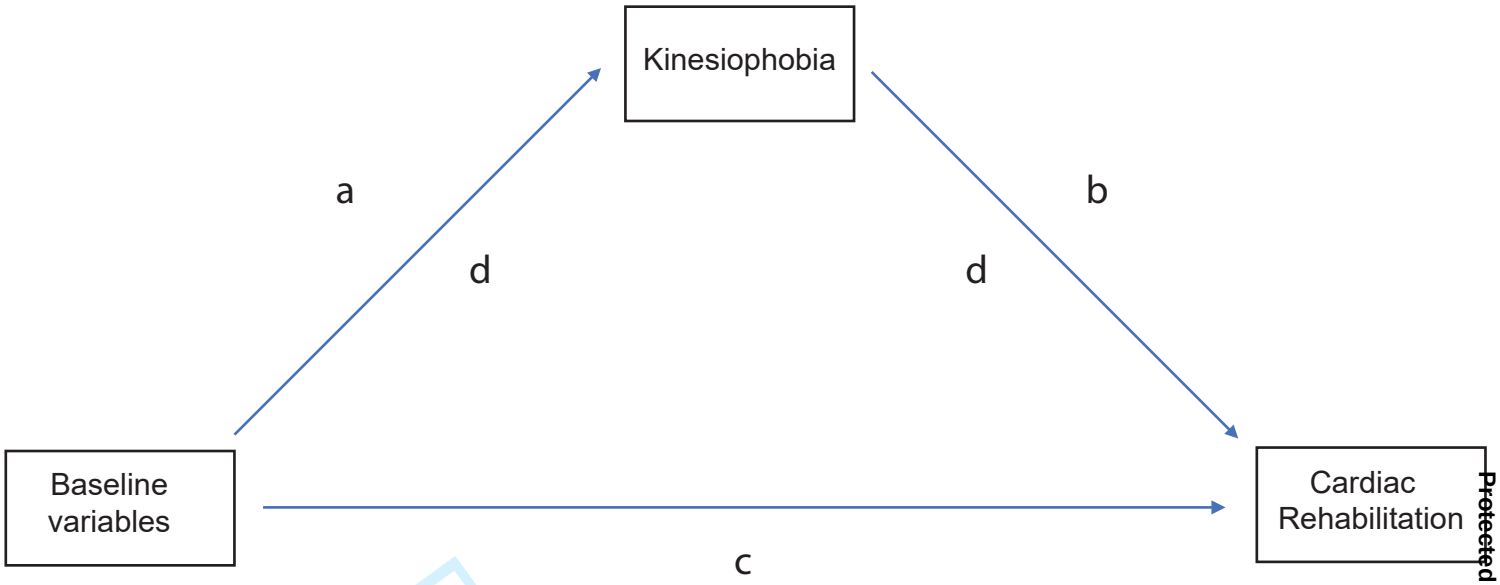


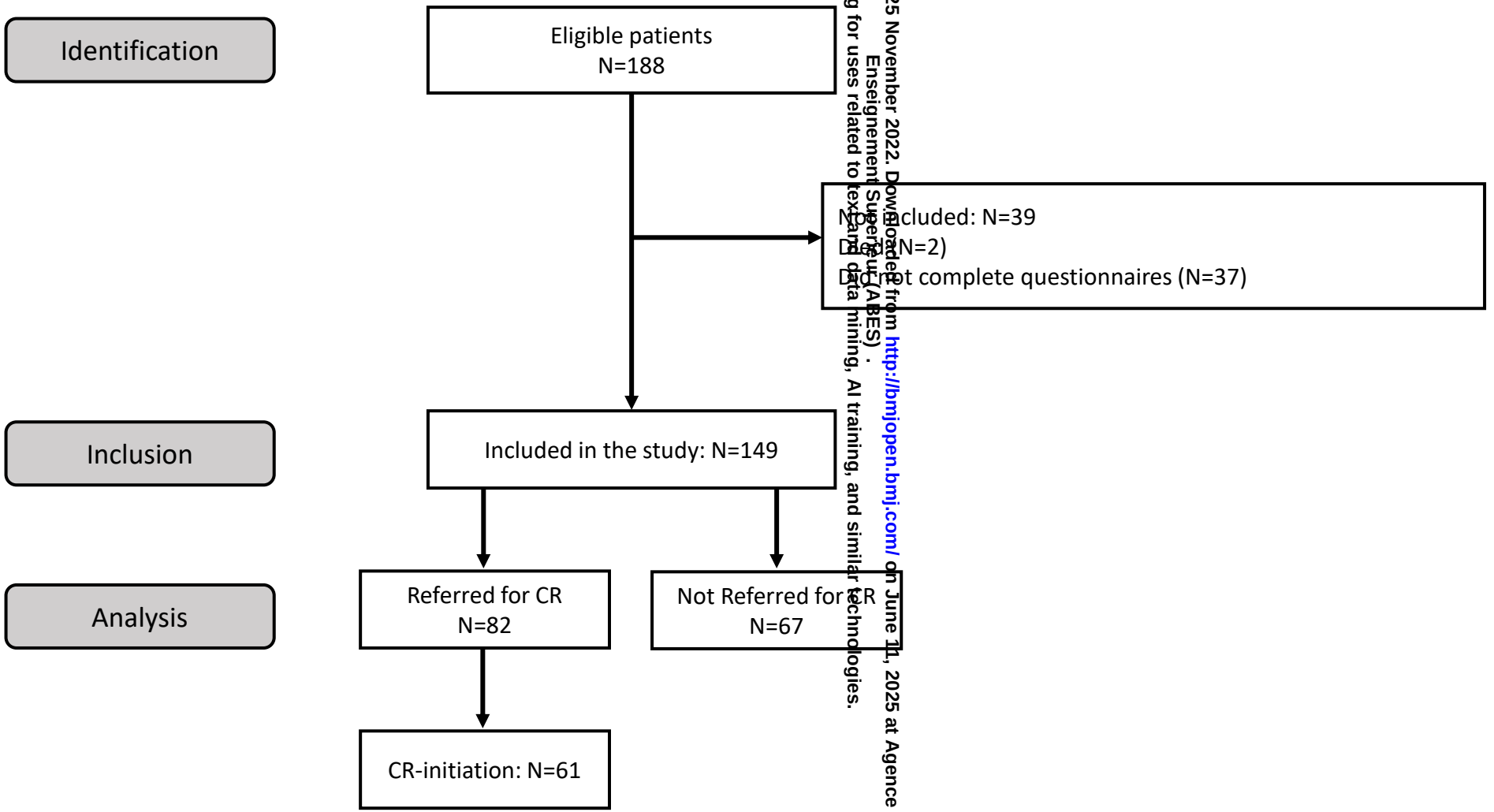
Analyses

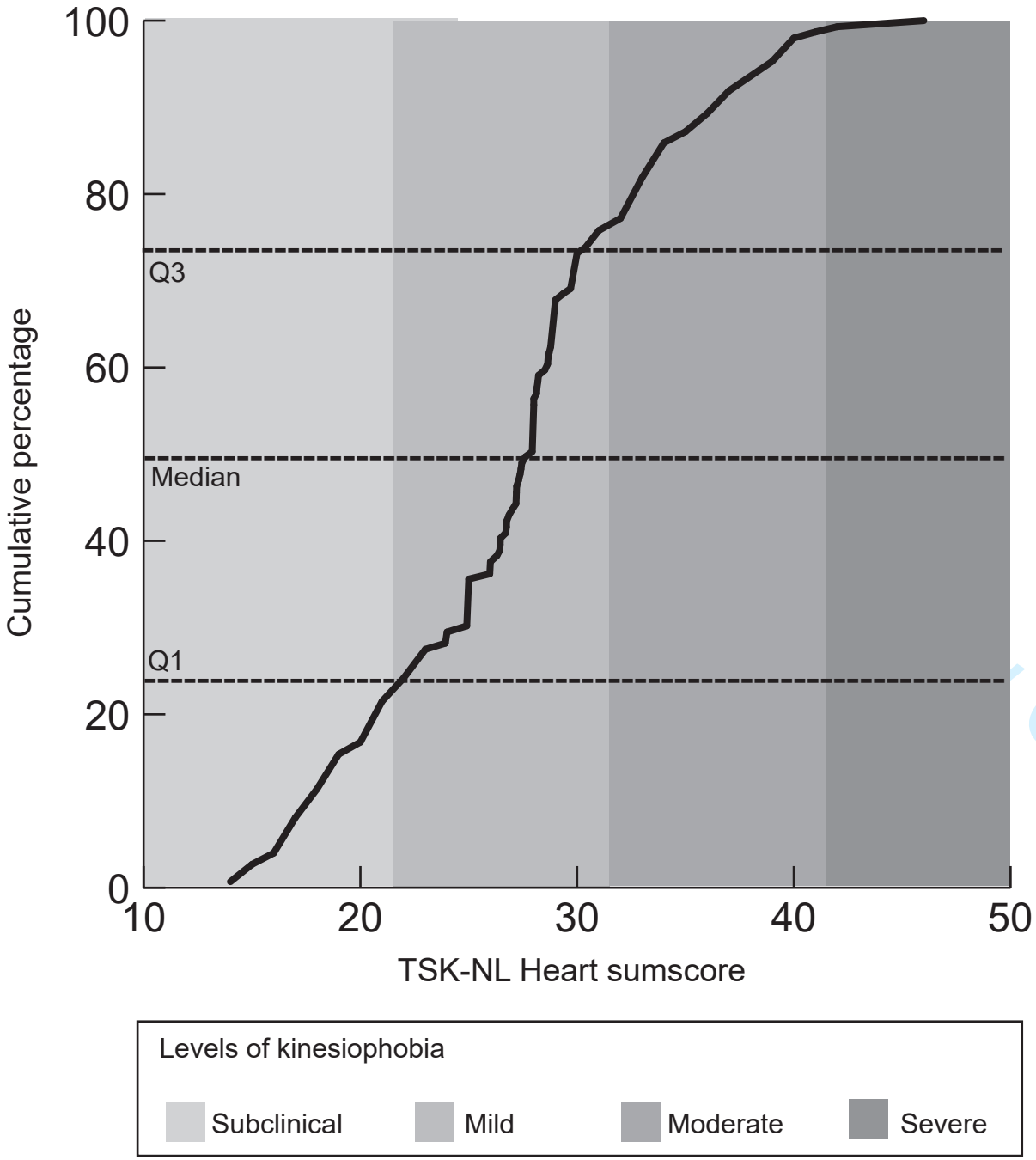
a. Direct effect of baseline variables on kinesiophobia.

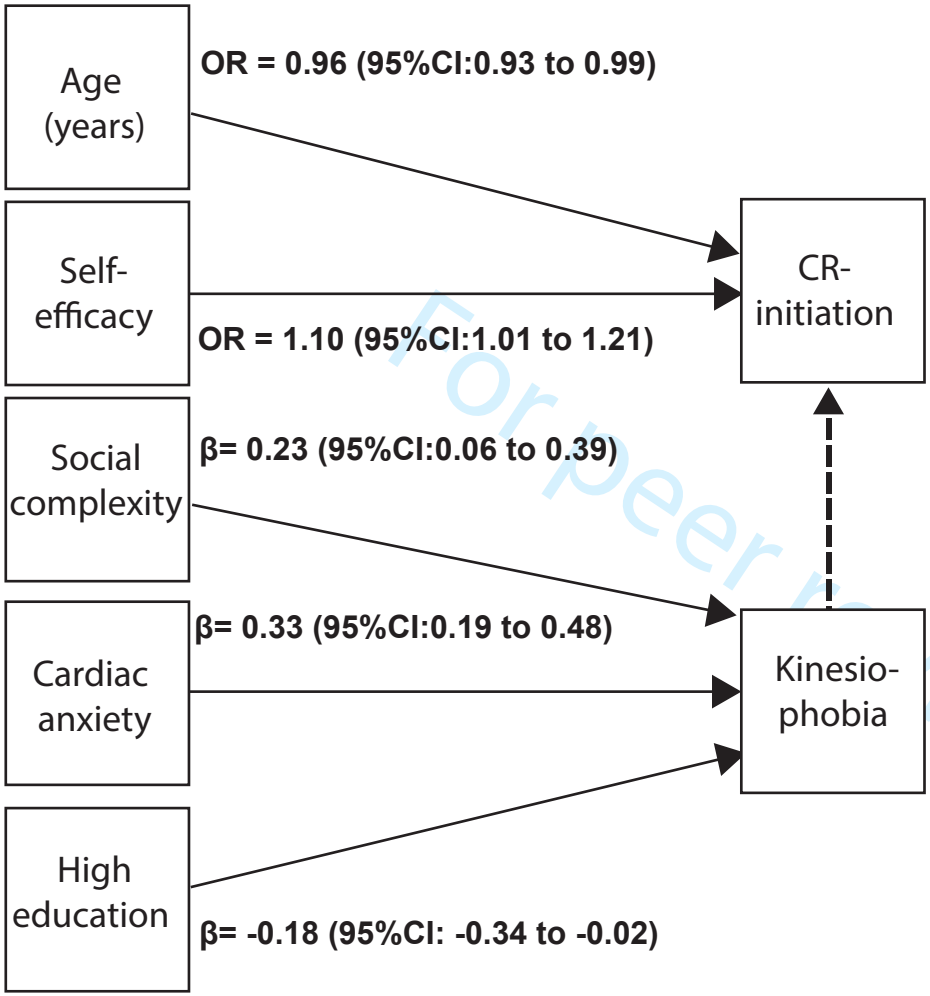
b. Direct effect of kinesiophobia on CR-initiation.

c. Direct effect of baseline variables on CR-initiation.

d. Indirect effect of baseline variables on CR-initiation, with kinesiophobia as mediator.







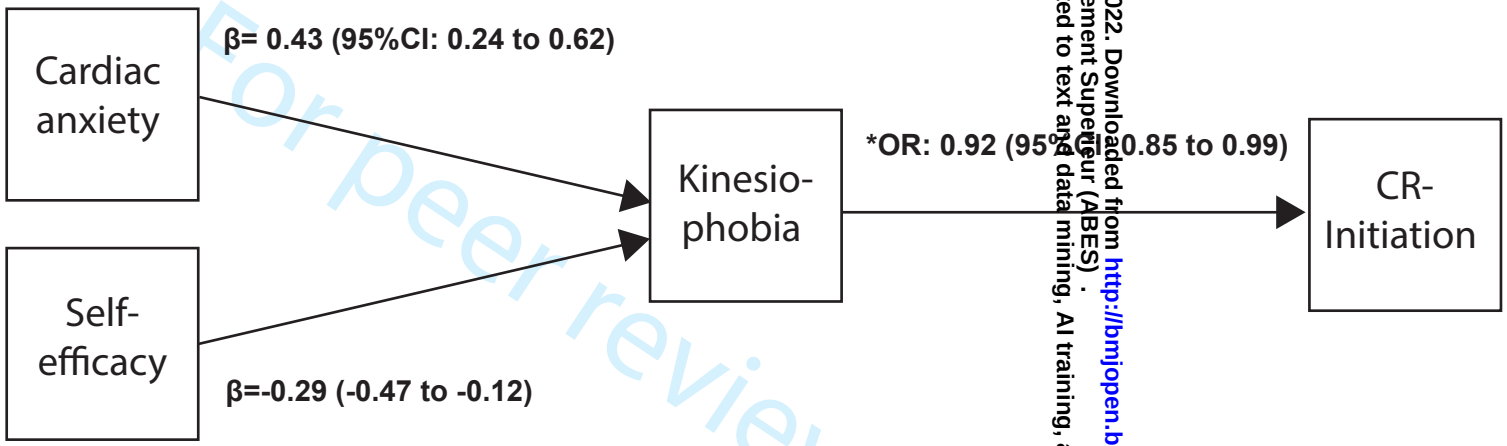


Table 1: Statistical analyses

Variable	Data type	Missing data (%)	Regressed on outcome: 1. TSK NL- Heart 2. CR initiation
Demographics			
Age	Continuous	-	1+2
Female Sex	Binary	-	1+2
Higher Education	Binary	-	1+2
Index event			
Acute coronary syndrome	Binary	-	1+2
Stable angina revascularization	Binary	-	1+2
Atrial Fibrillation	Binary	-	1+2
Admission			
Acute admission	Binary	-	1+2
Treatment index event			1+2
PCI	Binary	-	1+2
ECV	Binary	-	1+2
Medication only	Binary	-	1+2
Cardiac disease history			
Acute coronary syndrome	Binary	-	1+2
PCI	Binary	-	1+2
CABG	Binary	-	1+2
Stroke	Binary	-	1+2
Peripheral artery disease	Binary	-	1+2
CVD risk factors			
Diabetes mellitus	Binary	-	1+2
History of hypertension	Binary	-	1+2
History of dyslipidaemia	Binary	-	1+2
BMI	Continuous	-	1+2
Psychological risk factors			
GSES General Self-Efficacy scale	Continuous	26 (17.4)	1+2
HADS Anxiety	Continuous	26 (17.4)	1+2
HADS Depression	Continuous	26 (17.4)	1+2
IMSA Biological complexity	Continuous	28 (18.8)	1+2
IMSA Psychological complexity	Continuous	28 (18.8)	1+2
IMSA Social complexity	Continuous	28 (18.8)	1+2

CAQ Cardiac anxiety	Continuous	25 (16.8)	1+2
Outcomes variables			
Cardiac rehabilitation initiation	Binary	-	-
TSK Tampa Scale for Kinesiophobia	Continuous	34 (22.8)	2

Missing data analyses

This study was part of a large project were data were collected at 4 timepoints (hospital discharge, 3 weeks, 6 weeks and 12 weeks). Patients were included in the analyses if they completed the TSK-Heart NL questionnaire on, at least, one of the aforementioned timepoints. In total, 149 patients were included in the analyses. Missing values of the TSK-NL Heart were: Hospital discharge: 34 (22.8%), 3 weeks 37: (24.8%), 6 weeks: 42 (28.2%), 12 weeks: 54 (36.2%). Little's MCAR test was used to determine patterns of missing data. (Little's MCAR Test Chi Square = 4871,310 DF= 4995, Sig =0.893). A full conditional model (FCS MI) was used to impute data in m=5 datasets. FCS MI is a powerful method to create multiple imputations in datasets with categorical and continuous variables and is well suited for datasets with complex structures [1].

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Table 3: Univariable logistic regression with CR initiation in the Total sample and subsample referred for CR

	Total Sample (N=149)				Referred for CR (N= 82)	
Variable	**CR-initiation No (N=88)**	**CR-initiation Yes (N=61)**	**OR (95%CI)**	**P-value***	**OR (95%CI)**	**P-value***
Demographics						
Median age	66(48.0)	63(19.0)	0.96 (0.93 to 0.99)	0.02	0.98 (0.94 to 1.03)	0.49
Female sex (%)	21 (14.1)	11 (7.4)	0.70 (0.31 to 1.59)	0.40	0.44 (0.14 to 1.35)	0.15
Higher education (%)	68 (45.6)	42 (28.2)	0.65 (0.31 to 1.36)	0.25	0.52 (0.15 to 1.76)	0.29
Index event						
Acute coronary syndrome (%)	33 (22.1)	30 (20.1)	1.61 (0.83 to 3.13)	0.16	2.42 (0.83 to 7.07)	0.11
Stable angina revascularization (%)	35 (23.5)	23 (15.5)	0.92 (0.47 to 1.79)	0.8x	1.21 (0.43 to 3.22)	0.72
Atrial Fibrillation (%)	18 (12.1)	7 (4.7)	0.50 (0.20 to 1.29)	0.15	0.21 (0.07 to 0.69)	0.01
Admission type						
Acute admission (%)	35 (23.5)	31(20.8)	1.56 (0.81 to 3.02)	0.18	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	9 (6.0)	6 (4.0)	0.96 (0.32 to 2.85)	0.94	2.18 (0.25 to 19.26)	0.48
Treatment index event						
PCI (%)	65 (43.6)	52 (34.9)	2.04 (0.87 to 4.80)	0.10	3.56 (1.15 to 11.0)	0.03
ECV (%)	17 (11.4)	7 (4.7)	0.54 (0.21 to 1.40)	0.21	0.21 (0.07 to 0.69)	0.10
Medication only (%)	6 (4.0)	2 (1.3)	0.46 (0.09 to 2.38)	0.36	-	-
Cardiac disease history						
Acute coronary syndrome (%)	20 (13.5)	15 (10.1)	1.09 (0.51 to 2.35)	0.82	1.96 (0.51 to 7.58)	0.33
PCI (%)	34 (22.8)	22 (14.8)	0.90 (0.46 to 1.76)	0.75	0.75 (0.27 to 2.07)	0.58
CABG (%)	1 (0.7)	4 (2.7)	6.11 (0.67 to 56.02)	0.11	-	-
Stroke (%)	12 (8.1)	2 (1.3)	0.22 (0.05 to 0.99)	0.05	0.32 (0.04 to 2.45)	0.27
Peripheral artery disease (%)	8 (5.4)	2 (1.3)	0.34 (0.07 to 1.66)	0.18	0.68 (0.06 to 7.88)	0.76
CVD risk factors						
Diabetes Mellitus (%)	15 (10.1)	11 (7.4)	1.07 (0.45 to 2.52)	0.88	0.94 (0.26 to 3.33)	0.92
History of hypertension (%)	38 (25.5)	23 (15.4)	0.80 (0.41 to 1.55)	0.50	0.98 (0.35 to 2.73)	0.98
History of dyslipidemia (%)	20 (13.4)	19 (12.8)	1.54 (0.74 to 3.21)	0.25	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.28 (1.42)	27.03 (1.20)	1.01 (0.88 to 1.15)	0.91	0.96 (0.78 to 1.18)	0.69
Psychological risk factors						
Median TSK Kinesiophobia (IQR)	27.73 (10.50)	27.93 (93)	0.99 (0.95 to 1.05)	0.93	0.92 (0.85 to 1.00)	0.06
Median GSES Self Efficacy (IQR)	32.86 (4.84)	33.49 (7.00)	1.11 (1.01 to 1.21)	0.02	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	4.29 (4.17)	5.39 (4.99)	0.92 (0.84 to 1.00)	0.06	0.89 (0.79 to 1.00)	0.06
Median HADS Depression	4.65 (4.32)	4.00 (5.70)	0.96 (0.87 to 1.06)	0.44	0.93 (0.81 to 1.06)	0.27
Median IMSA Biological complexity	14.27 (3.00)	15.00 (4.00)	0.99 (0.90 to 1.09)	0.92	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.00 (3.07)	5.42 (2.81)	0.87 (0.74 to 1.02)	0.09	0.82 (0.66 to 1.00)	0.06
Median IMSA Social complexity	7.79 (3.00)	8.64 (3.00)	1.08 (0.93 to 1.24)	0.32	1.02 (0.83 to 1.27)	0.84
CAQ Cardiac anxiety	26 (10.50)	27 (11.00)	0.99 (0.95 to 1.02)	0.44	0.97 (0.91 to 1.03)	0.36

In the total sample (N = 149) univariable logistic regression analyses revealed 6 candidate predictors of CR-initiation: Age (OR: 0.96 95% CI: 0.93 to 0.99), HADS anxiety (OR: 0.92 95% CI: 0.84 to 1.00) and IMSA psychological vulnerability (OR: 0.88 95% CI: 0.74 to 1.02) decreased the odds of CR-initiation. Treatment with PCI (OR: 2.04 95% CI: 0.87 to 4.80) and GSES Self-efficacy (OR: 1.11 95% CI: 1.01 to 1.21) increased the odds of CR-initiation.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1 +2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	7-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-18

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-18
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17
Discussion			
Key results	18	Summarise key results with reference to study objectives	19-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Impact of kinesiophobia on initiation of cardiac rehabilitation: a prospective cohort path analysis.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-066435.R1
Article Type:	Original research
Date Submitted by the Author:	13-Sep-2022
Complete List of Authors:	Keessen, Paul; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health; Amsterdam UMC Locatie AMC, Heart Center Kan, Kees-Jan; University of Amsterdam, Research Institute of Child Development and Education Ter Riet, Gerben; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Visser, Bart; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Jorstad, Harald; Amsterdam UMC - Locatie AMC, heart centre Latour, Corine; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health van Duijvenbode , Ingrid; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Scholte op Reimer , Wilma; Amsterdam UMC Locatie AMC, Department of Cardiology
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	REHABILITATION MEDICINE, Anxiety disorders < PSYCHIATRY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Impact of kinesiophobia on initiation of cardiac rehabilitation: a prospective cohort path analysis.

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Word count

Abstract: 283

Manuscript: 3024

References: 32

Keywords: kinesiophobia, fear of movement, cardiac rehabilitation, physical activity, path analysis, self-efficacy

Journal: BMJ Heart

ABSTRACT

Objectives: To identify factors associated with kinesiophobia (fear of movement) after cardiac hospitalization and to assess the impact of kinesiophobia on CR-initiation.

Design: Prospective cohort study

Setting: Academic Medical Centre, department of Cardiology

Participants: We performed a prospective cohort study in cardiac patients recruited at hospital discharge. In total, 149 patients (78.5% male) with a median age of 65 years were included, of which 82 (59%) were referred for cardiac rehabilitation (CR).

Primary and secondary outcome measures: We assessed kinesiophobia with the Tampa Scale for Kinesiophobia (TSK). For this study the total score was used (range 13-52). We assessed baseline factors (demographics, cardiac disease history, questionnaire data on anxiety, biopsychosocial complexity and self-efficacy) associated with kinesiophobia using linear regression with backward elimination. For linear regression the standardized beta (β) was reported. Prospectively, the impact of kinesiophobia on probability of CR-initiation, in the first 3 months after hospital discharge (subsample referred for CR), was assessed with logistic regression. For logistic regression the odds ratio (OR) was reported.

Results: Moderate and severe levels of kinesiophobia were found in 22.8%. In the total sample, kinesiophobia was associated with cardiac anxiety (β=0.33 95%CI: 0.19 to 0.48), social complexity (β=0.23 95%CI: 0.06 to 0.39) and higher education (β=-0.18 95%CI:-0.34 to -0.02). In those referred for CR, kinesiophobia was negatively associated with self-efficacy (β = -0.29 95% CI: -0.47 to -0.12) and positively with cardiac anxiety (β= 0.43 95%CI: 0.24 to 0.62). Kinesiophobia decreased the probability of CR-initiation ($OR^{Range13-52\ points}$ = 0.92 95%CI: 0.84 to 0.99).

Conclusion: In patients hospitalised for cardiovascular disease, kinesiophobia is associated with cardiac anxiety, social complexity, educational level and self-efficacy. Kinesiophobia decreased the likelihood of CR-initiation with 8% per point on the TSK.

Strengths and limitations of this study

- Little is known about Kinesiophobia at (or shortly after) hospital discharge.
- This study describes the impact of kinesiophobia on initiation of cardiac rehabilitation (CR).
- Using a path analysis gives insight in factors that are associated with kinesiophobia and predict CR-initiation.
- Findings from this study can be used to guide the development of early interventions to improve kinesiophobia and CR-initiation.
- This observational study does not permit any claims with regard to causal inference

INTRODUCTION

Fear of movement (kinesiophobia) is present in 45% of patients with cardiovascular disease (CVD) at the start of cardiac rehabilitation (CR) and remains present in 20% of patients after 3-10 months after hospital discharge. Kinesiophobia is associated with decreased quality of life and low levels of physical activity (PA) [1][2][3]. Moreover, kinesiophobia negatively impacts the uptake of CR, despite CR's proven benefits such as reduced morbidity and mortality, and better psychological wellbeing [4][5][6].

The effect of kinesiophobia at hospital discharge on the uptake of CR has not been prospectively investigated. Previous qualitative research has shown that patients attribute high levels of kinesiophobia to a lack of support and information at hospital discharge from a health care provider [3]. Insight in factors associated with kinesiophobia at hospital discharge, and how kinesiophobia impacts CR-initiation, could help to identify potential determinants of kinesiophobia, which in turn could potentially impact CR-initiation, and help to adequately support and refer those with kinesiophobia.

Therefore the aims of this study were to explore (1) factors associated with kinesiophobia at hospital discharge and (2) the impact of kinesiophobia on initiation of CR.

METHODS

Study design

We performed a prospective cohort study, in patients hospitalised with CVD, from hospital discharge up to 3 months follow-up. To explore factors associated with kinesiophobia and the effect of kinesiophobia on CR-initiation, a hypothetical path-model was developed (explained in detail below) **(Figure 1).** Patients were included at hospital discharge (or shortly after) from the Amsterdam University Medical Centre at the department of Cardiology.

fig1:hypotheticalpathmodel

Ethics consideration

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Patient population

Eligible patients had been hospitalized for acute coronary syndrome (ACS), stable angina pectoris (AP), acute heart failure (AHF) or atrial fibrillation (AF). Exclusion criteria were: referral to a nursing home; inability to complete questionnaires, e.g. due to language problems.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Sample size considerations

Based on previous research we expected to include 10 variables in our final path-model [2]. We therefore aimed to include 15 times the number of parameters in our study, resulting in a final sample size of 150 patients [7].

Data collection and measurements

Patients were identified between August 2019 and May 2021 through the electronic health records system of the Amsterdam University Medical Centers. During hospitalisation, eligible

patients were interviewed by study staff of the Amsterdam University of Applied Sciences and enrolled in this study if they consented. The following data were collected from the electronic health record: age, sex, educational level, marital status, cardiac diagnosis and disease history. Patients were asked by email to complete questionnaires about their biopsychosocial complexity, the level of self-efficacy, anxiety and depression at discharge.

Outcomes

The primary outcomes were kinesiophobia at hospital discharge and CR-initiation (yes/no) 3 months after discharge. At hospital discharge, patients completed the Tampa Scale for Kinesiophobia (TSK-NL Heart). The TSK-NL Heart consists of 13 questions with a four-point scale ranging from 1 to 4, with a minimum score of 13 and maximum score of 52 points. Scores on the TSK-NL Heart are categorized as follows: subclinical: 13–22; mild: 23–32; moderate: 33–42; and severe: 43–52 [1]. After 3 months patients were asked, by telephone, if they 1) were referred for CR, 2) initiated CR 3) were readmitted to the hospital for an unplanned procedure.

Self-reported measurements

All self-reported measurements were completed during, or shortly after, hospital discharge (maximum 2 days).

Biopsychosocial complexity

Patients' biopsychosocial complexity was assessed with the Intermed Self-Assessment (IMSA). The IMSA has four domains: biological complexity (chronicity and severity of symptoms, complications and life threat), psychological complexity (restrictions in coping, resistance to treatment, mental health threat, psychiatric dysfunction) and social complexity (social dysfunction, residential instability). Scores >19 indicate high complexity [8]. In this study, the biological, psychological and social domains were analysed separately.

Generic anxiety and depression

Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale

(HADS). A sum score of 8-10 is defined as `possible anxiety/depressive disorder', a sum score of 11-21 is defined as `likely anxiety/depression disorder' [9].

Cardiac anxiety

The cardiac anxiety questionnaire (CAQ) is an 18-item, self-report questionnaire, designed to measure cardiac anxiety (fear, attention, avoidance of physical exercise and safety-seeking behaviour), rated on a 5-point Likert scale ranging from 0 (never) to 4 (always) [10].

Self-efficacy

Self-efficacy was assessed with the General Self-Efficacy Scale (GSES). The GSES is a 10 item questionnaire with a four-point Likert scale ranging from 0 (completely disagree) to 4 (completely agree). A higher sum score indicates better self-efficacy [11].

Statistical analysis

Descriptive statistics

Patient characteristics are presented as median and interquartile range (IQR) or numbers (%). We analysed baseline kinesiophobia and differences between patients based on CR-referral and CR- initiation. In addition, we assessed which patients were readmitted to the hospital for acute coronary syndrome, revascularization or electro-cardioversion within the period of this study (3 months).

Path analysis

We explored direct effects (relations between independent and dependent variables) and indirect effects (the effect of an independent variable on a dependent variable through one or more intervening or mediating variables) [12] **(Figure 1).** Since little is known about kinesiophobia in patients with CVD, a comprehensive approach was used to explore the association between baseline variables, kinesiophobia and the initation of CR. We studied the association between demographic variables (age, sex, educational level), medical variables (diagnosis, cardiac disease history, risk factors), psychological variables (biopsychosocial complexity, generic anxiety, cardiac anxiety, self-efficacy) and

kinesiophobia. Categorical variables were recoded into dummy variables (educational level, diagnosis, cardiac disease history, risk factors). All other variables (age, BMI, kinesiophobia, psychological variables). were analysed as continuous. In addition, we studied the longitudinal association between kinesiohobia, the abovementioned demographic, medical, psychological variables and CR-initiation. An overview of all analyses is found in online **appendix 1, table 1.**

First, univariable linear regression was used to select variables associated with kinesiophobia (TSK-NL Heart total score). Univariable logistic regression was used to select variables associated with CR-initiation in a subsample that was referred for CR (cut-off for variable retainment in both analyses: P<0.10) [13]. Second, a path analysis was conducted. Backward elimination was used to select significant (P<0.05) variables associated with kinesiophobia. The initiation of CR (yes/no) was regressed on kinesiophobia to study the direct effect of kinesiophobia on CR-initiation and possible indirect effects of baseline variables on CR-initiation, with kinesiophobia as mediator. Path analyses were conducted for the total sample and in a subsample that was referred for CR.

All effects on kinesiophobia (continuous TSK-NL Heart score) are presented as standardized beta estimates (β). Effect size of (β) was interpreted as small (<0.29), moderate (0.30 - 0.49), large (> 0.50) [14]. Effects on the uptake of CR are presented as odds ratios. In the final model, the effect of kinesiophobia on CR-initiation was corrected for age and gender. The Satorra-Bentler scaled chi square test (X^2) was used to assess model fit. Patterns of missing data were analysed with Little's test to assess the pattern of missing data. A full conditional specification Multiple Imputation (FCS MI) [15]. Data-imputation was conducted in SPSS V28. An overview of all missing data is found in **Online Appendix 1, Table 1.** All descriptive and univariable analyses were performed in SPSS V28. The path models were analysed using Mplus V8.0.

RESULTS

Demographic and clinical characteristics

In total, 188 patients were assessed for eligibility. After inclusion, 39 patients (20.7%) did not complete any questionnaires, and 2 died. At hospital discharge, 82 (55%) patients were referred for CR, of which 61 (40.9%) initiated CR in 3 months follow up **(figure 2).**

fig2:flowchartstudy

Finally, 149 patients were included in the analyses with a median age of 65 years (range 32-86). The majority of patients were male (78.5%) and lived with a partner (77.9%). Most patients had been admitted for an elective intervention (55.7%), of which 78.5% underwent a Percutaneous Coronary Intervention (PCI). A history of hypertension was present in 40.9%, dyslipidaemia in 26.2% and diabetes mellitus in 17.4. Prior myocardial infarction was present in 23.4% and prior PCI (acute or elective) in 37.6% **(table 1).** The distribution of kinesiophobia levels were: subclinical (24.2%), mild (53.0%), moderate (22.1%) and severe (0.7%) **(figure 3).**

Baseline TSK-scores were, on average, 3 points higher in patients that were referred but did not initiate CR, than in those who did initiate CR (30.39 ± SD 6.76 vs 27.37 ± SD 5.98). Within 3 months follow up, 15 patients (10%) were readmitted to the hospital: 6 patients for Electro Cardioversion (ECV), 6 patients for PCI, 2 patients for ACS and 1 patient for acute heart failure.

fig3:kinesiophobiascores

Table 1: Baseline characteristics

(N=149)	
Demographics	
Age, years, mean (SD)	65.5 (14)
Male (%)	117 (78.5)
Higher education (%)	39 (26.2)
Lives with partner (%)	116 (77.9)
Index event (%)	
Acute Coronary Syndrome	
STEMI	32 (21.5)
NSTEMI	22(14.8)
UAP	9 (6.0)
Stable Angina revascularization	58 (38.9)
Acute Heart Failure	3 (2.0)
Atrial Fibrillation	25 (16.7)
Admission type (%)	
Acute admission	66 (44.3)
Elective admission	83 (55.7)
Treatment for index event (%)	
PCI	117 (78.5)
ECV	24 (16.1)
Medication only	8 (5.4)
Cardiac disease history (%)	
Myocardial infarction	35 (23.4)
PCI	56 (37.6)
CABG	5 (3.4)
Stroke	14 (9.4)
Peripheral artery disease	10 (6.7)
Cardiovascular disease risk factors [b] (%)	
Diabetes Mellitus type 2	26 (17.4)
History of hypertension	61 (40.9)
History of dyslipidaemia	39 (26.2)
BMI category (kg/m^2)	
18- 25	16 (10.8)
25-30	120 (80.5)
>30	13 (8.7)

[a] Multiple diagnoses possible

Values presented as median (IQR) and counts (%)

STEMI: ST-Elevation Myocardial Infarction,

NSTEMI: Non ST-Elevation Myocardial Infarction,

UAP: Unstable Angina Pectoris,

PCI: Percutaneous Coronary Intervention,

ECV: Electro Cardio Version,

CABG: Coronary Artery Bypass Grafting,

BMI: Body Mass Index.

Univariable analyses

An overview of all our univariable linear regression analyses is presented in **table 2.** We found small associations between kinesiophobia and female sex (β= 0.19 95% CI: 0.03 to 0.35) , Age ≤ 50 (β = 0.22 95% CI: 0.38 to 2.49), and HADS anxiety (β = 0.27 95% CI: 0.11 to 0.42). Higher education (β=-0.24 95% CI: -0.40 to -0.08) and GSES self-efficacy (β=-0.18 95% CI: -0.34 to -0.02) were negatively associated with kinesiophobia. Moderate associations were found between kinesiophobia and HADS Depression (β=0.32 95% CI:0.16 to 0.47), IMSA psychological complexity (β = 0.32 95% CI: 0.17 to 0.48), IMSA social complexity (β=0.33 95% CI: 0.17 to 0.48) and CAQ cardiac anxiety (β=0.42 95% CI: 0.27 to 0.57).

Table 2: Univariable Linear regression with TSK-NL Heart as dependent variable (N=149)

Variable	Standardized Beta (95% CI)	Adjusted R-square	P-value
Demographics			
Age (continuous)	-0.13 (-0.29 to 0.04)	0.001	0.13
Age ≤ 50	0.22 (0.38 to 2.49)	0.05	0.008
Female Sex	0.19 (0.03 to 0.35)	0.03	0.02
Higher Education	-0.24 (-0.40 to -0.08)	0.05	0.003
Index event			
Acute coronary syndrome	0.08 (-0.08 to 0.25)	0.001	0.31
Stable angina revascularization	-0.04 (-0.21 to 0.12)	-0.001	0.61
Atrial Fibrillation	-0.04 (-0.21 to 0.12)	-0.001	0.59
Admission			
Acute admission	0.07 (-0.09 to 0.24)	0.001	0.37
Treatment index event			
PCI	0.02 (-0.14 to 0.19)	-0.01	0.79
ECV	-0.02 (-0.19 to 0.14)	-0.01	0.99
Medication only	-0.01 (-0.16 to 0.16)	-0.01	0.99
Cardiac disease history			
Acute coronary syndrome	-0.08 (-0.25 to 0.08)	0.001	0.32
PCI	0.001 (-0.16 to 0.16)	-0.001	0.49
CABG	0.06 (-0.10 to 0.22)	-0.001	0.46
Stroke	-0.11 (-0.28 to 0.49)	0.001	0.17
Peripheral artery disease	0.03 (-0.13 to 0.20)	-0.001	0.40
CVD risk factors			
Diabetes mellitus	-0.02 (-0.18 to 0.15)	-0.001	0.83
History of hypertension	0.03 (-0.13 to 0.20)	-0.01	0.69
History of dyslipidaemia	0.08 (-0.09 to 0.24)	-0.001	0.35
BMI	0.14 (-0.19 to 0.30)	0.01	0.08
Psychological risk factors			
GSES General Self-Efficacy scale	-0.18 (-0.34 to -0.02)	0.03	0.03
HADS Anxiety	0.27 (0.11 to 0.42)	0.06	0.001
HADS Depression	0.32 (0.16 to 0.47)	0.09	0.001
IMSA Biological complexity	0.21 (0.06 to 0.37)	0.04	0.009
IMSA Psychological complexity	0.32 (0.17 to 0.48)	0.10	0.001
IMSA Social complexity	0.33 (0.17 to 0.48)	0.10	0.001
CAQ Cardiac anxiety	0.42 (0.27 to 0.57)	0.17	0.001

GSES: General Self Efficacy Scale, HADS: Hospital Anxiety and Depression Scale, IMSA: InterMed Self-Assessment, CAQ: Cardiac Anxiety Questionnaire

In patients referred for CR (N=82), 9 candidate predictors of CR-initiation were found. TSK Kinesiophobia (OR: 0.92 95% CI: 0.85 to 1.00), treatment with ECV (OR:0.21 95% CI: 0.07 to 0.69), atrial fibrillation (OR: 0.21 95% CI: 0.07 to 0.69), HADS anxiety (OR: 0.89 95% CI: 0.79 to 1.00), HADS depression (OR:0.93 95%CI: 0.81 to 1.06), and IMSA psychological complexity (OR: 0.82 95% CI: 0.66 to 1.00) decreased the odds of CR initiation. Treatment with PCI (OR: 3.56 95% CI: 1.15 to 11:00), acute admission (OR: 2.58 95% CI: 0.89 to 7.54) and GSES Self-efficacy (OR: 1.18 95% CI: 1.03 to 1.36) increased the odds for CR initiation **(table 3).** In those referred for CR, 7 patients were readmitted to the hospital for an unplanned procedure, of which 6 initiated CR (OR: 2.18 95%CI: 0.32 to 2.85). An overview of all candidate predictors of CR in the total sample (N=149) is found in **Online Appendix 2 Table 2.**

Table 3: Univariable logistic regression with CR initiation as dependent variable in a subsample referred for CR (N=82)

Variable	CR-initiation No (N=21)	CR-initiation Yes (N=61)	OR (95% CI)	P-value
Demographics				
Age	63 (11.0)	63 (19.0)	0.98 (0.94 to 1.01)	0.49
Age ≤ 50	1 (1.2)	12 (14.6)	4.90 (0.60 to 40.22)	0.14
Age >50	20 (24.4)	49 (59.8)	0.20 (0.03 to 1.66)	0.14
Female sex (%)	7 (33.3)	11 (18.0)	0.44 (0.14 to 1.36)	0.14
Higher education (%)	16 (23.9)	19 (31.1)	1.92 (0.57 to 6.46)	0.29
Index event				
Acute coronary syndrome (%)	6 (28.6)	30 (49.2)	2.42 (0.83 to 7.11)	0.11
Stable angina revascularization (%)	7 (33.3)	23 (37.7)	1.21 (0.43 to 3.44)	0.72
Atrial fibrillation (%)	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.68)	0.01
Admission type				
Acute admission index event	6 (4.0)	31 (20.8)	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	1 (4.8)	6 (9.8)	2.18 (0.25 to 19.22)	0.48
Treatment index event				
PCI	13 (61.9)	52 (85.2)	3.56 (1.49 to 16.00)	0.03
ECV	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.69)	0.10
Medication only	-	2 (3.3)	-	-
Cardiac disease history				
Acute coronary syndrome	3 (14.3)	15 (24.6)	1.96 (0.51 to 7.58)	0.33
PCI	9 (42.9)	22 (36.1)	0.75 (0.27 to 2.07)	0.58
CABG	-	4 (6.6)	-	-
Stroke	2 (9.5)	2 (3.3)	0.33 (0.42 to 2.45)	0.27
Peripheral artery disease	1 (4.8)	2 (3.3)	0.68 (0.06 to 7.38)	0.76
CVD risk factors				
Diabetes Mellitus (%)	4 (19.0)	11 (18.0)	0.94 (0.26 to 3.33)	0.92
Hypertension (%)	8 (38.1)	23 (37.7)	0.98 (0.35 to 2.73)	0.98
Dyslipidemia (%)	5 (23.8)	19 (31.1)	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.07 (1.16)	27.02 (1.20)	0.96 (0.78 to 1.18)	0.69
Psychological risk factors				
Median TSK Kinesiophobia (IQR)	29.00 (10.78)	27.93 (7.00)	0.92 (0.85 to 1.00)	0.06
Median GSES Self-Efficacy (IQR)	32.67 (5.50)	33.49(7.00)	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	7.00 (4.00)	5.39(4.99)	0.89 (0.79 to1.00)	0.06
Median HADS Depression (IQR)	5.00 (5.21)	4.00(5.70)	0.93 (0.81 to1.06)	0.06
Median IMSA Biological complexity	14 (2.63)	15 (4.00)	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.64(4.0)	5.42(2.81)	0.82 (0.66 to1.00)	0.06
Median IMSA Social complexity (IQR)	7.89 (3.50)	8.64 (3.00)	1.02 (0.83 to 1.27)	0.84
Median CAQ Cardiac Anxiety	26.45 (7.00)	27.00 (11.00)	0.97 (0.92 to 1.03)	0.36

Path analysis

Analysis 1: Total sample

In the total sample we identified three variables that were associated with kinesiophobia **(table 4).** CAQ cardiac anxiety (β = 0.33 95% CI: 0.19 to 0.48) was moderately associated with kinesiophobia. A small association was found between kinesiophobia and IMSA social complexity (β = 0.23 95% CI: 0.06 to 0.39) and higher education (β = -0.18 95% CI: -0.34 to -0.02). We identified two predictors of CR-initiation: age (years) (OR: 0.96 95% CI: 0.93 to 0.99) decreased, while higher levels of GSES self-efficacy (OR: 1.10 95% CI: 1.01 to 1.20) increased the odds for CR-initiation. An overview of all variables associated with kinesiophobia and CR-initiation are presented in a path analysis diagram **(figure 4).**

Model fit (X^2= -2.254124, DF:0.972, P = 1.00).

fig4:pathmodeltotal

Table 4: Path analysis with TSK and CR as dependent variables (N=149)

Dependent variable: TSK		
Variable	**Standardized Beta (95% CI)**	**P-value**
CAQ Cardiac anxiety	0.33 (0.19 to 0.48)	0.001
IMSA Social complexity	0.23 (0.06 to 0.39)	0.006
Higher Education	-0.18 (-0.34 to -0.02)	0.03
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
Age	0.96 (0.93 to 0.99)	0.02
GSES Self-Efficacy	1.10 (1.01 to 1.20)	0.03

Analysis 2: Subsample referred for CR

In the subsample that was referred for CR, we identified two variables that were associated with kinesiophobia **(table 5).** A moderate positive association was found between CAQ cardiac anxiety (β = 0.43 95% CI: 0.24 to 0.62) and kinesiophobia, while GSES self-efficacy (β=-0.29 95% CI: -0.47 to -0.12) was negatively associated with kinesiophobia. Age (OR= 0.98 95% CI: 0.94 to 1.02) was kept in the model since model fit decreased after omission of this variable and age <50 was significantly associated with kinesiophobia and initiation of CR **(table 2)** and **(online appendix 2).** Corrected for age, kinesiophobia (OR=0.92 95% CI: 0.84 to 0.99) significantly decreased the odds of CR-initiation. A moderate indirect effect of CAQ cardiac anxiety (OR = 0.98 95% CI: 0.95 to 1.00) on CR-initiation was found with kinesiophobia as a mediator. The subsample analysis is presented in a path analysis diagram **(figure 5).** Model fit (X^2= -0.0062, DF: 0.973, P = 1.00).

fig5:pathmodelsubsample

Table 5: Path analysis with TSK and CR- initiation as dependent variables, restricted to patients who had been referred to CR (N=82)

Dependent variable: TSK		
Variable	**Standardized Beta (95%CI)**	**P-value**
CAQ Cardiac anxiety	0.43 (0.24 to 0.62)	0.001
GSES Self-Efficacy	-0.29 (-0.47 to -0.12)	0.001
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
TSK Kinesiophobia		
Model a	0.92 (0.85 to 0.99)	0.05
Model b	0.92 (0.84 to 0.99)	0.04
Model c	0.93 (0.86 to 1.01)	0.08
Model c+d	0.92 (0.85 to 1.01)	0.07
Mediation analysis: indirect effect of cardiac anxiety an self-efficacy on CR-initiation with TSK as mediator		
Variable	**OR (95%CI)**	**P-value**
CAQ Cardiac Anxiety	0.98 (0.95 to 1.00)	0.05
GSES Self-efficacy	1.04 (0.99 to 1.09)	0.11

a = Crude association b = Corrected for age, c = Corrected for gender, d = Corrected for age + gender

DISCUSSION

We found that mild and moderate levels of kinesiophobia were present at hospital discharge in a substantial group of patients with CVD (53% and 22.1% respectively). Cardiac anxiety, social complexity, and educational level were associated with kinesiophobia at hospital discharge. In patients who were referred for CR, self-efficacy was negatively associated with kinesiophobia. In patients referred for CR, the presence of kinesiophobia was associated with a lower rate of CR initiation. An indirect effect of cardiac anxiety on CR-initiation was found.

Our study shows that kinesiophobia decreases the likelihood of CR initiation. Theoretically this makes sense since the construct kinesiophobia comprises `fear of injury', `perception of risk' and `avoidance of physical activity'. Patients with higher levels of kinesiophobia might associate participation in CR as threatening since exercise and physical activity are the cornerstones of CR.

We identified a moderate association between cardiac anxiety and kinesiophobia. In a previous study a similar result was found [1]. Moreover, we found that kinesiophobia mediated the relationship between cardiac anxiety and CR-initiation. This finding is in line with previous research which reports that kinesiophobia mediates the relationship between self-rated anxiety and CR-attendance [4]. The CAQ measures behaviour and anxiety-related symptoms (e.g. *"I avoid activities that make my heart beat faster"*) whereas the TSK-NL Heart measures patients' beliefs about their physical state (e.g. *"If I tried to be physically active my heart problem would increase"*). More research is needed to investigate the impact of specific kinesiophobic beliefs on behaviour and anxiety related symptoms and vice versa.

In line with our findings, Brunetti et al, showed that educational level was negatively associated with kinesiophobia [16]. In a previous study, we found that patients with high levels of kinesiophobia often do not understand medical information and misinterpret body signals, which in turn is associated with poor health literacy and low educational level [3][17].

This finding fits well with the call for more tailored and understandable information at hospital discharge, provided by a trained healthcare provider [3].

Patients scoring high on social complexity suffered from higher levels of kinesiophobia. This is in line with our previous study where we found that patients with lower levels of kinesiophobia often experienced greater social support than those with higher levels of kinesiophobia [3]. The presence of a partner has been shown to improve lifestyle modification in cardiac patients and increase adherence to CR [18]. Moreover, participation of partners in CR-programs improves PA-levels in patients [19][20]. Future studies should evaluate the role of social support on levels of kinesiophobia after cardiac hospitalization.

Self-efficacy was negatively associated with kinesiophobia, in those referred for CR, and predicted CR-initiation in the total sample. Self-efficacy refers to `one's belief in their capacity to execute behaviours necessary to produce specific performance attainments' [21]. The association between self-efficacy and kinesiophobia has been shown in patients with musculoskeletal disorders, but not in patients with CVD [22][23]. Zelle et al., reported that the impact of kinesiophobia on physical activity is largely mediated by self-efficacy, and should therefore be evaluated when targeting kinesiophobia [24]. Our study showed that self-efficacy increased the likelihood of CR-initiation by 10%. Self-efficacy is linked to CR-initiation, but is often lacking in patients with psychological distress [25]. Therefore, self-efficacy-building activities should be considered *before* CR-initiation [26]. Currently, behaviour change strategies are offered in CR-programs to improve PA levels, promote smoking cessation and a healthy diet [27]. However, these interventions are currently limited to those that initiate CR. An early behavioural intervention, aimed at reducing kinesiophobia and stimulating self-efficacy shorty after hospital discharge might improve CR-initiation.

Strengths and limitations

Our study has several strengths. First, we studied kinesiophobia and CR-initiation using a prospective design. We were therefore able to study the temporal sequence of kinesiophobia

and CR-initiation, and multiple factors that impacted our outcomes. Second, using a path model allows for the specification of multiple, dependent and independent variables simultaneously and thereby gives insight into complex relationships between variables [12]. Our comprehensive path analysis gives insight in the factors that are associated with kinesiophobia and predict CR-initiation. These findings aid the development of tailored interventions to target kinesiophobia and improve CR-initiation.

Our study has some limitations. First, a substantial number of patients were included after the start of the COVID-19 pandemic. Although CR was offered remotely, this might have impacted kinesiophobia levels and CR-initiation. Second, by using path analysis we were able to explore a network of sequential relations with contributions from all paths (direct and indirect). Conceptually, a mediation model (in contrast to a confounding model) assumes that a series of variables relate via a causal chain of effect and each variable in the model affects variables occurring later in the chain [28]. In our model, an indirect effect of cardiac anxiety, through kinesiophobia, was found on CR-initiation. Theoretically, our finding makes sense, since somatic symptoms such as chest pain or palpitations (cardiac anxiety), can lead to negative beliefs about one's physical state (kinesiophobia), which in turn might lead to not initiating CR. Future studies should evaluate the potential mediating role of kinesiophobia in the uptake of CR. Third, although our interest is in causes of kinesiophobia and kinesiophobia as a cause of not initiating CR, our observational study does not permit any claims with regard to causal inference since necessary conditions for causal inference (exchangeability, positivity and consistency) have most likely not been met [29]. Nevertheless, this study reports important associations between baseline variables and kinesiophobia. In addition, we showed that kinesiophobia decreased the likelihood of CR-initiation. Future studies, using a causal design can use these results to investigate determinants of kinesiophobia and the effect of kinesiophobia on CR-initiation.

CONCLUSION

Kinesiophobia is prevalent at hospital discharge. Path analysis revealed that cardiac anxiety

and social complexity were positively associated, whereas educational level, and self-efficacy were negatively associated with kinesiophobia at hospital discharge. In addition, patients with (high levels of) kinesiophobia were less likely to initiate CR.

Figure Legends

Figure 1: Hypothetical path model

Figure 2: Flowchart of study

Figure 3: Kinesiophobia scores at hospital discharge

Figure 4: Path analysis in total sample (N=149)

Figure 5: Path analysis in subsample referred for CR

Acknowledgement:

The authors are grateful to department of Cardiology of the Amsterdam University Medical Centre, all research nurses involved in the data collection and patients who participated in this study: Hiltje van der Werf, Manon Ootes, Marjon van Maarl and Willeke Veenhuizen.

Contributors:

GR, BV, HTJ, CHM and WSoR participated in the design of the study. PK and ICDvD were responsible for coordination and acquisition of the data. PK, KK and GR performed the statistical analysis. All authors contributed to the preparation, critical review and approved the final manuscript.

Funding:

Financial support was received from the Dutch Research Council (NWO) as a personal grant (PK; nr: 023.010.064) and a RAAK-PRO grant (RAAK.PRO02.083).

The funding bodies had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Data availability statement

Data are available on reasonable request. Requests for analyses of data from this study should be directed to: P Keessen (p.keessen@hva.nl).

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Conflict of interest

We have read and understood BMJ policy on declaration of interests and declare that we have no conflicting interests.

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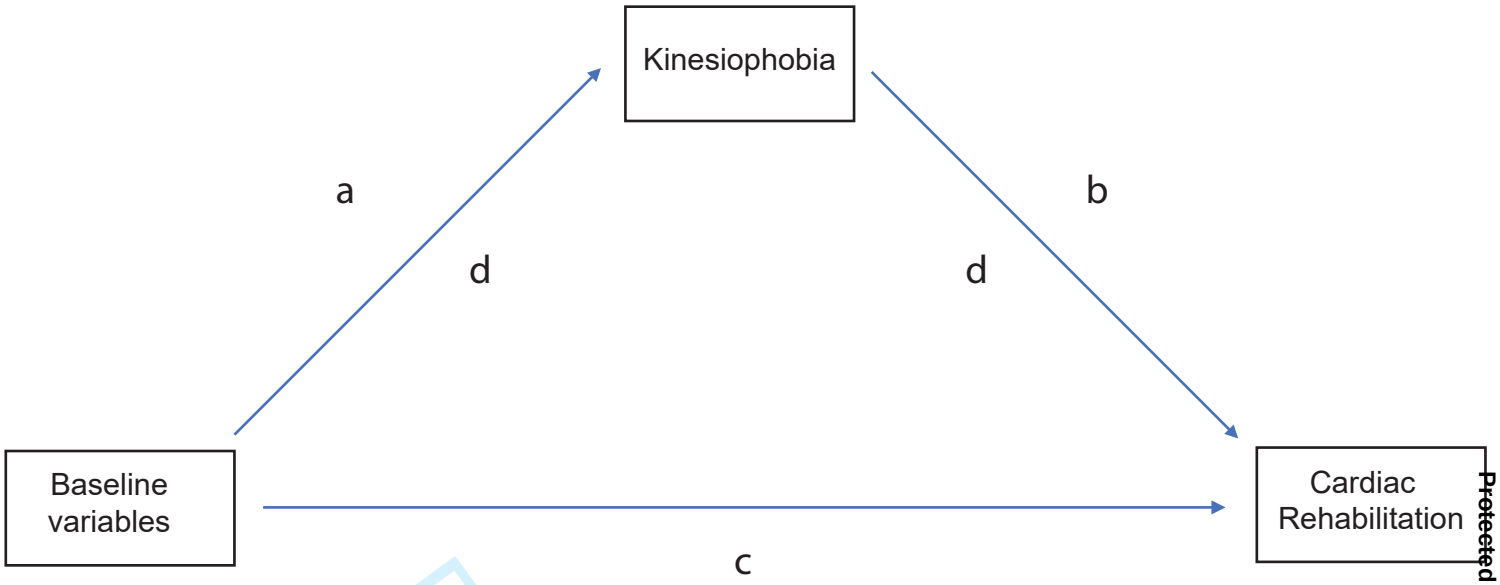


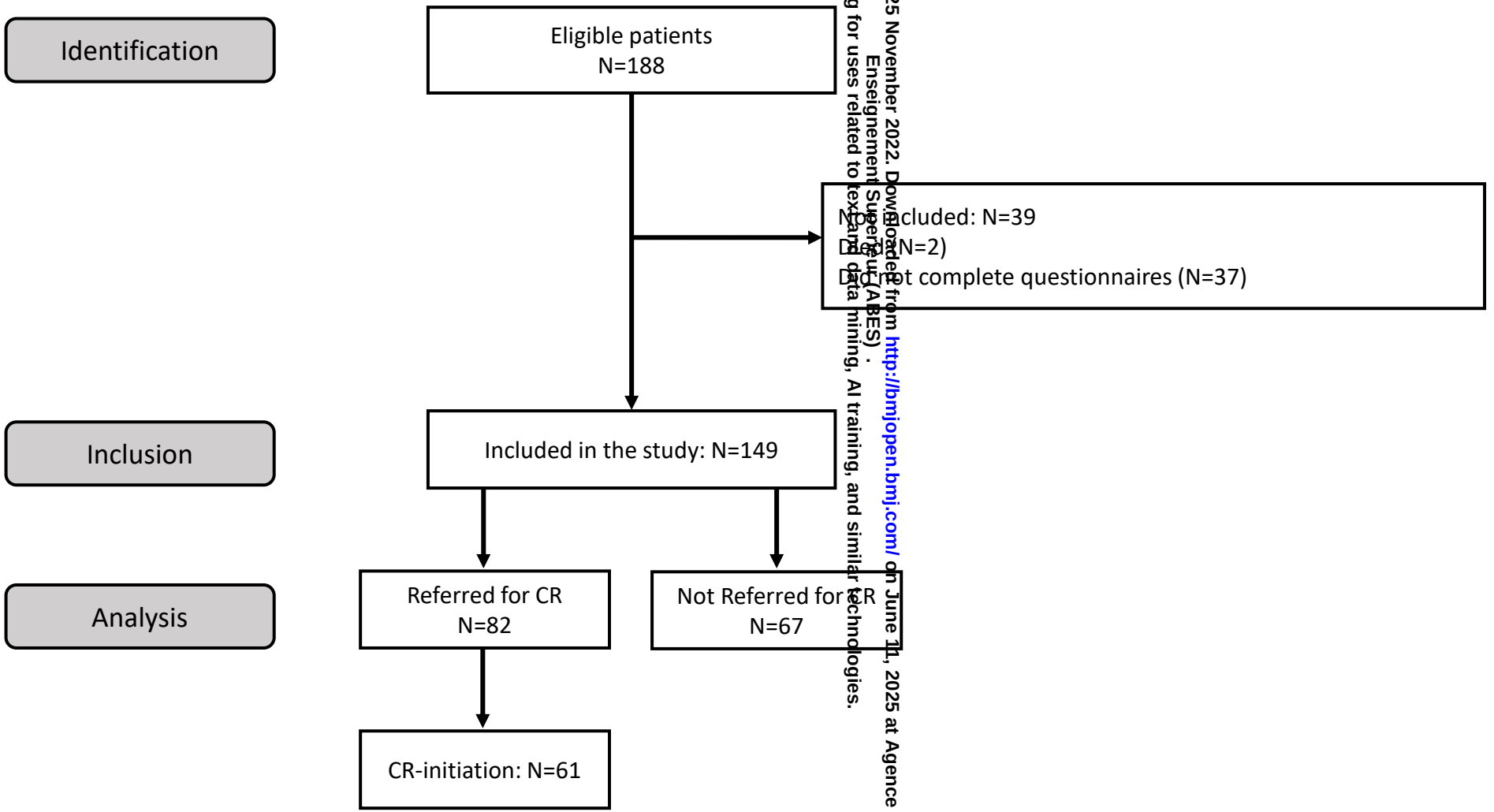
Analyses

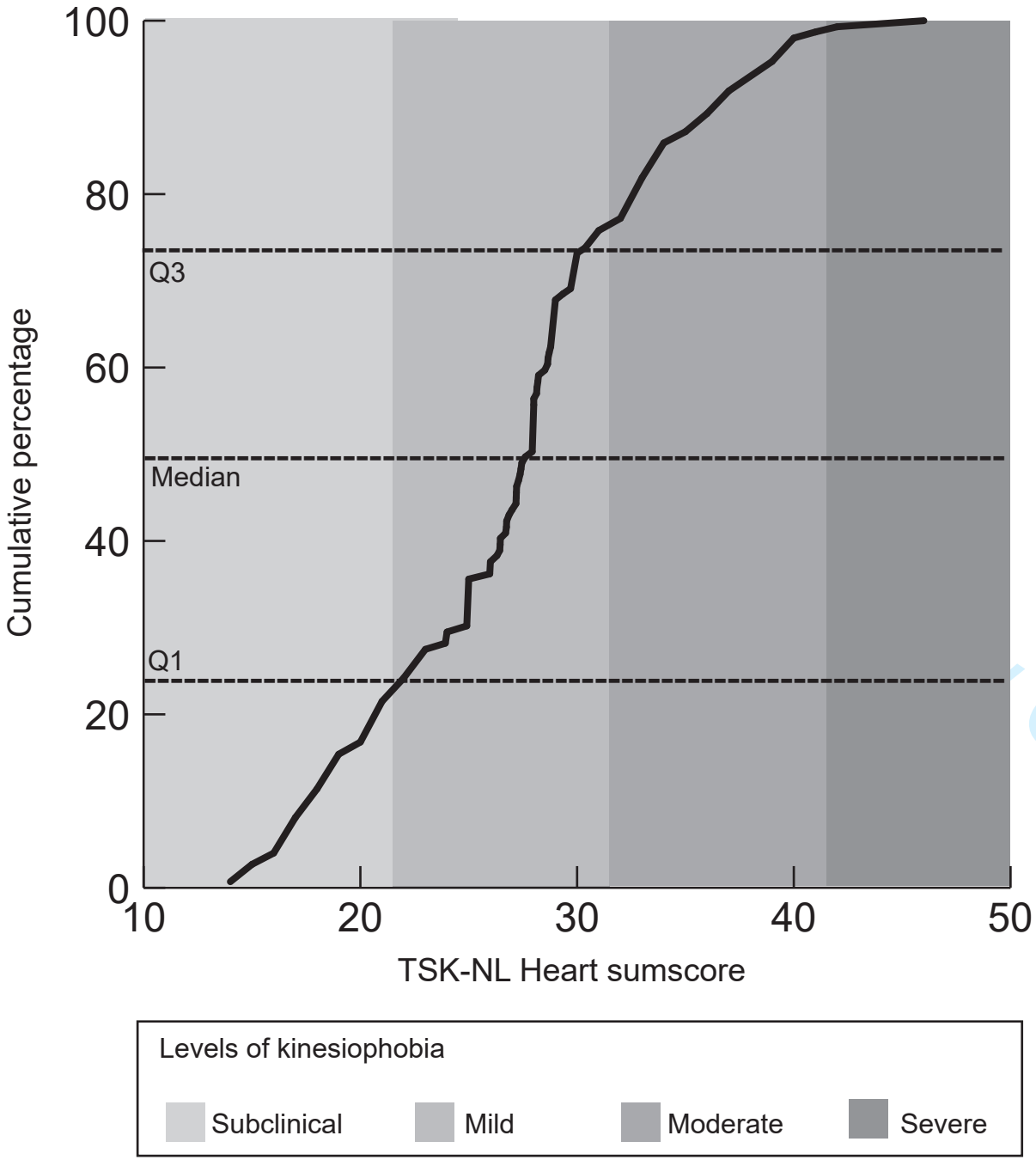
a. Direct effect of baseline variables on kinesiophobia.

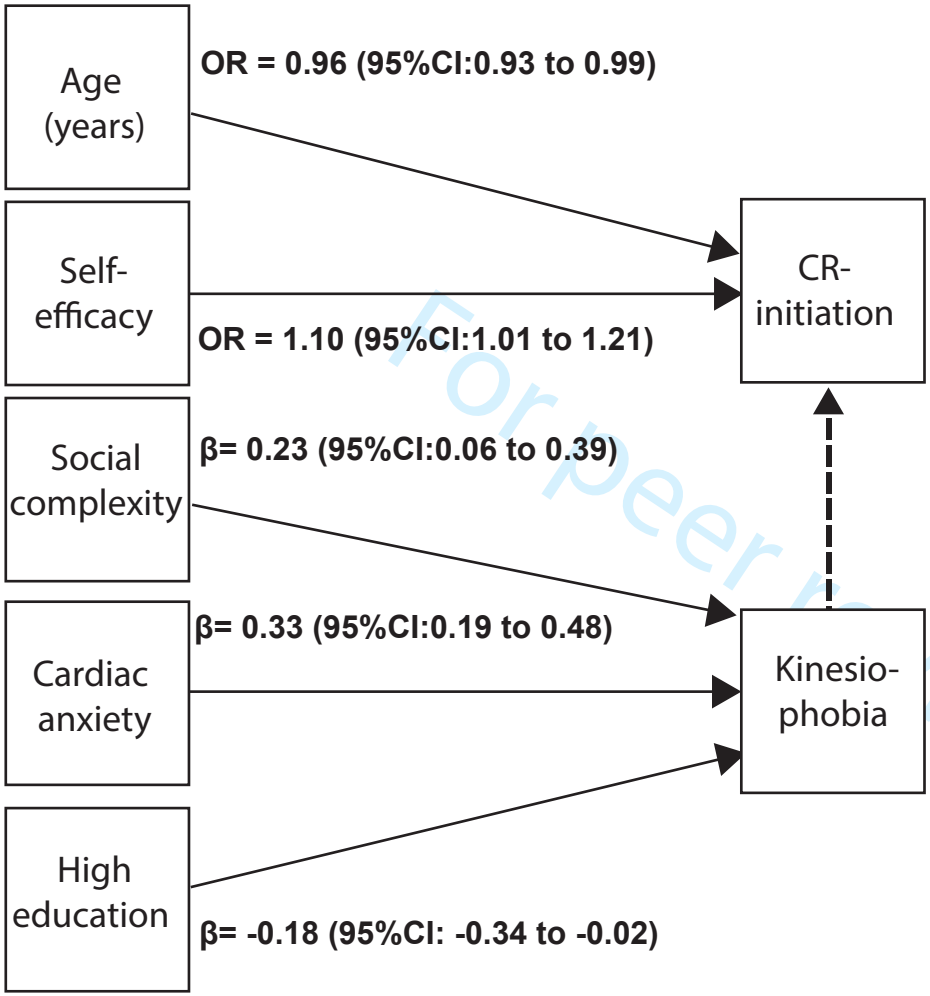
b. Direct effect of kinesiophobia on CR-initiation.

c. Direct effect of baseline variables on CR-initiation.

d. Indirect effect of baseline variables on CR-initiation, with kinesiophobia as mediator.







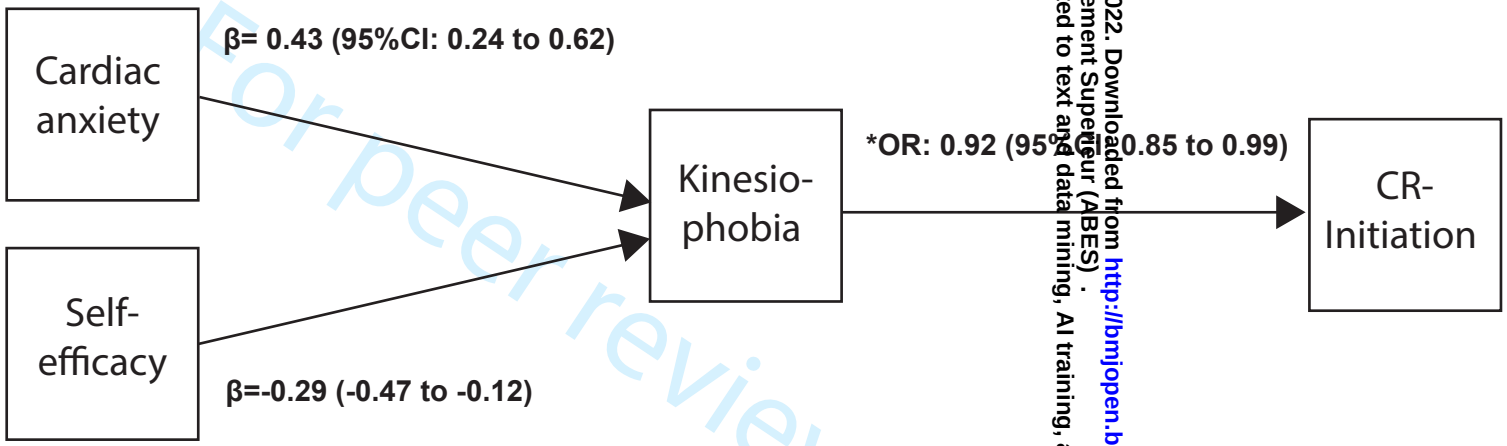


Table 1: Statistical analyses

Variable	Data type	Missing data (%)	Regressed on outcome: 1. TSK NL- Heart 2. CR initiation
Demographics			
Age	Continuous	-	1+2
Female Sex	Binary	-	1+2
Higher Education	Binary	-	1+2
Index event			
Acute coronary syndrome	Binary	-	1+2
Stable angina revascularization	Binary	-	1+2
Atrial Fibrillation	Binary	-	1+2
Admission			
Acute admission	Binary	-	1+2
Treatment index event			1+2
PCI	Binary	-	1+2
ECV	Binary	-	1+2
Medication only	Binary	-	1+2
Cardiac disease history			
Acute coronary syndrome	Binary	-	1+2
PCI	Binary	-	1+2
CABG	Binary	-	1+2
Stroke	Binary	-	1+2
Peripheral artery disease	Binary	-	1+2
CVD risk factors			
Diabetes mellitus	Binary	-	1+2
History of hypertension	Binary	-	1+2
History of dyslipidaemia	Binary	-	1+2
BMI	Continuous	-	1+2
Psychological risk factors			
GSES General Self-Efficacy scale	Continuous	26 (17.4)	1+2
HADS Anxiety	Continuous	26 (17.4)	1+2
HADS Depression	Continuous	26 (17.4)	1+2
IMSA Biological complexity	Continuous	28 (18.8)	1+2
IMSA Psychological complexity	Continuous	28 (18.8)	1+2
IMSA Social complexity	Continuous	28 (18.8)	1+2

CAQ Cardiac anxiety	Continuous	25 (16.8)	1+2
Outcomes variables			
Cardiac rehabilitation initiation	Binary	-	-
TSK Tampa Scale for Kinesiophobia	Continuous	34 (22.8)	2

Missing data analyses

This study was part of a large project where data were collected at 4 timepoints (hospital discharge, 3 weeks, 6 weeks and 12 weeks). Patients were included in the analyses if they completed the TSK-Heart NL questionnaire on, at least, one of the aforementioned timepoints. In total, 149 patients were included in the analyses. Missing values of the TSK-NL Heart were: Hospital discharge: 34 (22.8%), 3 weeks: 37 (24.8%), 6 weeks: 42 (28.2%), 12 weeks: 54 (36.2%). Little's MCAR test was used to determine patterns of missing data. (Little's MCAR Test Chi Square = 4871,310 DF= 4995, Sig =0.893). A full conditional model (FCS MI) was used to impute data in m=5 datasets. FCS MI is a powerful method to create multiple imputations in datasets with categorical and continuous variables and is well suited for datasets with complex structures [1].

1. Liu Y, De A. Multiple Imputation by Fully Conditional Specification for Dealing with Missing Data in a Large Epidemiologic Study. Int J Stat Med Res. 2015;4(3):287-295. doi: 10.6000/1929-6029.2015.04.03.7. Epub 2015 Aug 19. PMID: 27429686; PMCID: PMC4945131.

Table 2: Univariable logistic regression with CR initiation in the Total sample and subsample referred for CR

	Total Sample (N=149)				Referred for CR (N= 82)	
Variable	**CR-initiation No (N=88)**	**CR-initiation Yes (N=61)**	**OR (95%CI)**	**P-value***	**OR (95%CI)**	**P-value***
Demographics						
Median age	66(48.0)	63(19.0)	0.96 (0.93 to 0.99)	0.02	0.98 (0.94 to 1.03)	0.49
Female sex (%)	21 (14.1)	11 (7.4)	0.70 (0.31 to 1.59)	0.40	0.44 (0.14 to 1.35)	0.15
Higher education (%)	68 (45.6)	42 (28.2)	0.65 (0.31 to 1.36)	0.25	0.52 (0.15 to 1.76)	0.29
Index event						
Acute coronary syndrome (%)	33 (22.1)	30 (20.1)	1.61 (0.83 to 3.13)	0.16	2.42 (0.83 to 7.07)	0.11
Stable angina revascularization (%)	35 (23.5)	23 (15.5)	0.92 (0.47 to 1.79)	0.8x	1.21 (0.43 to 3.22)	0.72
Atrial Fibrillation (%)	18 (12.1)	7 (4.7)	0.50 (0.20 to 1.29)	0.15	0.21 (0.07 to 0.69)	0.01
Admission type						
Acute admission (%)	35 (23.5)	31(20.8)	1.56 (0.81 to 3.02)	0.18	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	9 (6.0)	6 (4.0)	0.96 (0.32 to 2.85)	0.94	2.18 (0.25 to 19.26)	0.48
Treatment index event						
PCI (%)	65 (43.6)	52 (34.9)	2.04 (0.87 to 4.80)	0.10	3.56 (1.15 to 11.0)	0.03
ECV (%)	17 (11.4)	7 (4.7)	0.54 (0.21 to 1.40)	0.21	0.21 (0.07 to 0.69)	0.10
Medication only (%)	6 (4.0)	2 (1.3)	0.46 (0.09 to 2.38)	0.36	-	-
Cardiac disease history						
Acute coronary syndrome (%)	20 (13.5)	15 (10.1)	1.09 (0.51 to 2.35)	0.82	1.96 (0.51 to 7.58)	0.33
PCI (%)	34 (22.8)	22 (14.8)	0.90 (0.46 to 1.76)	0.75	0.75 (0.27 to 2.07)	0.58
CABG (%)	1 (0.7)	4 (2.7)	6.11 (0.67 to 56.02)	0.11	-	-
Stroke (%)	12 (8.1)	2 (1.3)	0.22 (0.05 to 0.99)	0.05	0.32 (0.04 to 2.45)	0.27
Peripheral artery disease (%)	8 (5.4)	2 (1.3)	0.34 (0.07 to 1.66)	0.18	0.68 (0.06 to 7.88)	0.76
CVD risk factors						
Diabetes Mellitus (%)	15 (10.1)	11 (7.4)	1.07 (0.45 to 2.52)	0.88	0.94 (0.26 to 3.33)	0.92
History of hypertension (%)	38 (25.5)	23 (15.4)	0.80 (0.41 to 1.55)	0.50	0.98 (0.35 to 2.73)	0.98
History of dyslipidemia (%)	20 (13.4)	19 (12.8)	1.54 (0.74 to 3.21)	0.25	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.28 (1.42)	27.03 (1.20)	1.01 (0.88 to 1.15)	0.91	0.96 (0.78 to 1.18)	0.69
Psychological risk factors						
Median TSK Kinesiophobia (IQR)	27.73 (10.50)	27.93 (93)	0.99 (0.95 to 1.05)	0.93	0.92 (0.85 to 1.00)	0.06
Median GSES Self Efficacy (IQR)	32.86 (4.84)	33.49 (7.00)	1.11 (1.01 to 1.21)	0.02	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	4.29 (4.17)	5.39 (4.99)	0.92 (0.84 to 1.00)	0.06	0.89 (0.79 to 1.00)	0.06
Median HADS Depression	4.65 (4.32)	4.00 (5.70)	0.96 (0.87 to 1.06)	0.44	0.93 (0.81 to 1.06)	0.27
Median IMSA Biological complexity	14.27 (3.00)	15.00 (4.00)	0.99 (0.90 to 1.09)	0.92	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.00 (3.07)	5.42 (2.81)	0.87 (0.74 to 1.02)	0.09	0.82 (0.66 to 1.00)	0.06
Median IMSA Social complexity	7.79 (3.00)	8.64 (3.00)	1.08 (0.93 to 1.24)	0.32	1.02 (0.83 to 1.27)	0.84
CAQ Cardiac anxiety	26 (10.50)	27 (11.00)	0.99 (0.95 to 1.02)	0.44	0.97 (0.91 to 1.03)	0.36

In the total sample (N = 149) univariable logistic regression analyses revealed 6 candidate predictors of CR-initiation: Age (OR: 0.96 95% CI: 0.93 to 0.99), HADS anxiety (OR: 0.92 95% CI: 0.84 to 1.00) and IMSA psychological vulnerability (OR: 0.88 95% CI: 0.74 to 1.02) decreased the odds of CR-initiation. Treatment with PCI (OR: 2.04 95% CI: 0.87 to 4.80) and GSES Self-efficacy (OR: 1.11 95% CI: 1.01 to 1.21) increased the odds of CR-initiation.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1 +2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	7-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-18

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-18
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17
Discussion			
Key results	18	Summarise key results with reference to study objectives	19-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Impact of kinesiophobia on initiation of cardiac rehabilitation: a prospective cohort path analysis.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2022-066435.R2
Article Type:	Original research
Date Submitted by the Author:	26-Oct-2022
Complete List of Authors:	Keessen, Paul; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health; Amsterdam UMC Locatie AMC, Heart Center Kan, Kees-Jan; University of Amsterdam, Research Institute of Child Development and Education Ter Riet, Gerben; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Visser, Bart; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Jorstad, Harald; Amsterdam UMC - Locatie AMC, heart centre Latour, Corine; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health van Duijvenbode , Ingrid; Amsterdam University of Applied Sciences, Centre of Expertise Urban Vitality, Faculty of Health Scholte op Reimer , Wilma; Amsterdam UMC Locatie AMC, Department of Cardiology
Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	REHABILITATION MEDICINE, Anxiety disorders < PSYCHIATRY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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Impact of kinesiophobia on initiation of cardiac rehabilitation: a prospective cohort path analysis.

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Word count

Abstract: 283

Manuscript: 3024

References: 32

Keywords: kinesiophobia, fear of movement, cardiac rehabilitation, physical activity, path analysis, self-efficacy

Journal: BMJ Heart

ABSTRACT

Objectives: To identify factors associated with kinesiophobia (fear of movement) after cardiac hospitalization and to assess the impact of kinesiophobia on CR-initiation.

Design: Prospective cohort study

Setting: Academic Medical Centre, department of Cardiology

Participants: We performed a prospective cohort study in cardiac patients recruited at hospital discharge. In total, 149 patients (78.5% male) with a median age of 65 years were included, of which 82 (59%) were referred for cardiac rehabilitation (CR).

Primary and secondary outcome measures: We assessed kinesiophobia with the Tampa Scale for Kinesiophobia (TSK). For this study the total score was used (range 13-52). We assessed baseline factors (demographics, cardiac disease history, questionnaire data on anxiety, biopsychosocial complexity and self-efficacy) associated with kinesiophobia using linear regression with backward elimination. For linear regression the standardized beta (β) was reported. Prospectively, the impact of kinesiophobia on probability of CR-initiation, in the first 3 months after hospital discharge (subsample referred for CR), was assessed with logistic regression. For logistic regression the odds ratio (OR) was reported.

Results: Moderate and severe levels of kinesiophobia were found in 22.8%. In the total sample, kinesiophobia was associated with cardiac anxiety (β=0.33 95%CI: 0.19 to 0.48), social complexity (β=0.23 95%CI: 0.06 to 0.39) and higher education (β=-0.18 95%CI:-0.34 to -0.02). In those referred for CR, kinesiophobia was negatively associated with self-efficacy (β = -0.29 95% CI: -0.47 to -0.12) and positively with cardiac anxiety (β= 0.43 95%CI: 0.24 to 0.62). Kinesiophobia decreased the probability of CR-initiation ($OR^{Range13-52\ points}$ = 0.92 95%CI: 0.84 to 0.99).

Conclusion: In patients hospitalised for cardiovascular disease, kinesiophobia is associated with cardiac anxiety, social complexity, educational level and self-efficacy. Kinesiophobia decreased the likelihood of CR-initiation with 8% per point on the TSK.

Strengths and limitations of this study

- Structural Equation Modelling (SEM) was used to study direct and indirect effects.
- Path analysis allows the exploration of multiple dependent and independent variables simultaneously.
- A prospective study design was used to assess temporal relationships between variables.
- This observational study does not permit any claims with regard to causal inference

INTRODUCTION

Fear of movement (kinesiophobia) is present in 45% of patients with cardiovascular disease (CVD) at the start of cardiac rehabilitation (CR) and remains present in 20% of patients after 3-10 months after hospital discharge. Kinesiophobia is associated with decreased quality of life and low levels of physical activity (PA) [1][2][3]. Moreover, kinesiophobia negatively impacts the uptake of CR, despite CR's proven benefits such as reduced morbidity and mortality, and better psychological wellbeing [4][5][6].

The effect of kinesiophobia at hospital discharge on the uptake of CR has not been prospectively investigated. Previous qualitative research has shown that patients attribute high levels of kinesiophobia to a lack of support and information at hospital discharge from a health care provider [3]. Insight in factors associated with kinesiophobia at hospital discharge, and how kinesiophobia impacts CR-initiation, could help to identify potential determinants of kinesiophobia, which in turn could potentially impact CR-initiation, and help to adequately support and refer those with kinesiophobia.

Therefore the aims of this study were to explore (1) factors associated with kinesiophobia at hospital discharge and (2) the impact of kinesiophobia on initiation of CR.

METHODS

Study design

We conducted a prospective cohort study of patients hospitalized with a diagnosis of CVD, during the 3-month follow-up period after discharge. To explore factors associated with kinesiophobia and the effect of kinesiophobia on CR-initiation, a hypothetical path-model was developed (explained in detail below) **(Figure 1).** Patients were included at hospital discharge (or shortly after) from the Amsterdam University Medical Centre at the department of Cardiology.

fig1:hypotheticalpathmodel

Ethics consideration

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Patient population

Eligible patients had been hospitalized for acute coronary syndrome (ACS), stable angina pectoris (AP), acute heart failure (AHF) or atrial fibrillation (AF). Exclusion criteria were: referral to a nursing home; inability to complete questionnaires, e.g. due to language problems.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

Sample size considerations

Based on previous research we expected to include 10 variables in our final path-model [2]. We therefore aimed to include 15 times the number of parameters in our study, resulting in a final sample size of 150 patients [7].

Data collection and measurements

Patients were identified between August 2019 and May 2021 through the electronic health records system of the Amsterdam University Medical Centers. During hospitalisation, eligible patients were interviewed by study staff of the Amsterdam University of Applied Sciences and enrolled in this study if they consented. The following data were collected from the electronic health record: age, sex, educational level, marital status, cardiac diagnosis and disease history. Patients were asked by email to complete questionnaires about their biopsychosocial complexity, the level of self-efficacy, anxiety and depression at discharge.

Outcomes

The primary outcomes were kinesiophobia at hospital discharge and CR-initiation (yes/no) 3 months after discharge. At hospital discharge, patients completed the Tampa Scale for Kinesiophobia (TSK-NL Heart). The TSK-NL Heart consists of 13 questions with a four-point scale ranging from 1 to 4, with a minimum score of 13 and maximum score of 52 points. Scores on the TSK-NL Heart are categorized as follows: subclinical: 13–22; mild: 23–32; moderate: 33–42; and severe: 43–52 [1]. After 3 months patients were asked, by telephone, if they 1) were referred for CR, 2) initiated CR 3) were readmitted to the hospital for an unplanned procedure.

Self-reported measurements

All self-reported measurements were completed during, or shortly after, hospital discharge (maximum 2 days).

Biopsychosocial complexity

Patients' biopsychosocial complexity was assessed with the Intermed Self-Assessment (IMSA). The IMSA has four domains: biological complexity (chronicity and severity of symptoms, complications and life threat), psychological complexity (restrictions in coping, resistance to treatment, mental health threat, psychiatric dysfunction) and social complexity (social dysfunction, residential instability). Scores >19 indicate high complexity [8]. In this study, the biological, psychological and social domains were analysed separately.

Generic anxiety and depression

Anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS). A sum score of 8-10 is defined as `possible anxiety/depressive disorder', a sum score of 11-21 is defined as `likely anxiety/depression disorder' [9].

Cardiac anxiety

The cardiac anxiety questionnaire (CAQ) is an 18-item, self-report questionnaire, designed to measure cardiac anxiety (fear, attention, avoidance of physical exercise and safety-seeking behaviour), rated on a 5-point Likert scale ranging from 0 (never) to 4 (always) [10].

Self-efficacy

Self-efficacy was assessed with the General Self-Efficacy Scale (GSES). The GSES is a 10 item questionnaire with a four-point Likert scale ranging from 0 (completely disagree) to 4 (completely agree). A higher sum score indicates better self-efficacy [11].

Statistical analysis

Descriptive statistics

Patient characteristics are presented as median and interquartile range (IQR) or numbers (%). We analysed baseline kinesiophobia and differences between patients based on CR-referral and CR- initiation. In addition, we assessed which patients were readmitted to the hospital for acute coronary syndrome, revascularization or electro-cardioversion within the period of this study (3 months).

Path analysis

We explored direct effects (relations between independent and dependent variables) and indirect effects (the effect of an independent variable on a dependent variable through one or more intervening or mediating variables) [12] **(Figure 1).** Since little is known about kinesiophobia in patients with CVD, a comprehensive approach was used to explore the association between baseline variables, kinesiophobia and the initation of CR. We studied the association between demographic variables (age, sex, educational level), medical

variables (diagnosis, cardiac disease history, risk factors), psychological variables (biopsychosocial complexity, generic anxiety, cardiac anxiety, self-efficacy) and kinesiophobia. Categorical variables were recoded into dummy variables (educational level, diagnosis, cardiac disease history, risk factors). All other variables (age, BMI, kinesiophobia, psychological variables). were analysed as continuous. In addition, we studied the longitudinal association between kinesiohobia, the abovementioned demographic, medical, psychological variables and CR-initiation. An overview of all analyses is found in **Supplementary table 1.**

First, univariable linear regression was used to select variables associated with kinesiophobia (TSK-NL Heart total score). Univariable logistic regression was used to select variables associated with CR-initiation in a subsample that was referred for CR (cut-off for variable retainment in both analyses: $P<0.10$) [13]. Second, a path analysis was conducted. Backward elimination was used to select significant ($P<0.05$) variables associated with kinesiophobia. The initiation of CR (yes/no) was regressed on kinesiophobia to study the direct effect of kinesiophobia on CR-initiation and possible indirect effects of baseline variables on CR-initiation, with kinesiophobia as mediator. Path analyses were conducted for the total sample and in a subsample that was referred for CR.

All effects on kinesiophobia (continuous TSK-NL Heart score) are presented as standardized beta estimates (β). Effect size of (β) was interpreted as small (<0.29), moderate (0.30 - 0.49), large (> 0.50) [14]. Effects on the uptake of CR are presented as odds ratios. In the final model, the effect of kinesiophobia on CR-initiation was corrected for age and gender. The Satorra-Bentler scaled chi square test (X^2) was used to assess model fit. Patterns of missing data were analysed with Little's test to assess the pattern of missing data. A full conditional specification Multiple Imputation (FCS MI) [15]. Data-imputation was conducted in SPSS V28. An overview of all missing data is found in **Supplementary table 1.** All descriptive and univariable analyses were performed in SPSS V28. The path models were analysed using Mplus V8.0.

RESULTS

Demographic and clinical characteristics

In total, 188 patients were assessed for eligibility. After inclusion, 39 patients (20.7%) did not complete any questionnaires, and 2 died. At hospital discharge, 82 (55%) patients were referred for CR, of which 61 (40.9%) initiated CR in 3 months follow up **(figure 2).**

fig2:flowchartstudy

Finally, 149 patients were included in the analyses with a median age of 65 years (range 32-86). The majority of patients were male (78.5%) and lived with a partner (77.9%). Most patients had been admitted for an elective intervention (55.7%), of which 78.5% underwent a Percutaneous Coronary Intervention (PCI). A history of hypertension was present in 40.9%, dyslipidaemia in 26.2% and diabetes mellitus in 17.4. Prior myocardial infarction was present in 23.4% and prior PCI (acute or elective) in 37.6% **(table 1).** The distribution of kinesiophobia levels were: subclinical (24.2%), mild (53.0%), moderate (22.1%) and severe (0.7%) **(figure 3).**

Baseline TSK-scores were, on average, 3 points higher in patients that were referred but did not initiate CR, than in those who did initiate CR (30.39 ± 6.76 vs 27.37 ± 5.98). Within 3 months follow up, 15 patients (10%) were readmitted to the hospital: 6 patients for Electro Cardioversion (ECV), 6 patients for PCI, 2 patients for ACS and 1 patient for acute heart failure.

fig3:kinesiophobiascores

Table 1: Baseline characteristics

(N=149)	
Demographics	
Age, years, mean (SD)	65.5 (14)
Male (%)	117 (78.5)
Higher education (%)	39 (26.2)
Lives with partner (%)	116 (77.9)
Index event (%)	
Acute Coronary Syndrome	
STEMI	32 (21.5)
NSTEMI	22(14.8)
UAP	9 (6.0)
Stable Angina revascularization	58 (38.9)
Acute Heart Failure	3 (2.0)
Atrial Fibrillation	25 (16.7)
Admission type (%)	
Acute admission	66 (44.3)
Elective admission	83 (55.7)
Treatment for index event (%)	
PCI	117 (78.5)
ECV	24 (16.1)
Medication only	8 (5.4)
Cardiac disease history (%)	
Myocardial infarction	35 (23.4)
PCI	56 (37.6)
CABG	5 (3.4)
Stroke	14 (9.4)
Peripheral artery disease	10 (6.7)
Cardiovascular disease risk factors [b] (%)	
Diabetes Mellitus type 2	26 (17.4)
History of hypertension	61 (40.9)
History of dyslipidaemia	39 (26.2)
BMI category (kg/m^2)	
18- 25	16 (10.8)
25-30	120 (80.5)
>30	13 (8.7)

[a]

Multiple diagnoses possible
Values presented as median (IQR) and counts (%)
STEMI: ST-Elevation Myocardial Infarction,
NSTEMI: Non ST-Elevation Myocardial Infarction,
UAP: Unstable Angina Pectoris,
PCI: Percutaneous Coronary Intervention,
ECV: Electro Cardio Version,
CABG: Coronary Artery Bypass Grafting,
BMI: Body Mass Index.

Univariable analyses

An overview of all our univariable linear regression analyses is presented in **table 2.** We found small associations between kinesiophobia and female sex (β= 0.19 95% CI: 0.03 to 0.35) , Age ≤ 50 (β = 0.22 95% CI: 0.38 to 2.49), and HADS anxiety (β = 0.27 95% CI: 0.11 to 0.42). Higher education (β=-0.24 95% CI: -0.40 to -0.08) and GSES self-efficacy (β=-0.18 95% CI: -0.34 to -0.02) were negatively associated with kinesiophobia. Moderate associations were found between kinesiophobia and HADS Depression (β=0.32 95% CI:0.16 to 0.47), IMSA psychological complexity (β = 0.32 95% CI: 0.17 to 0.48), IMSA social complexity (β=0.33 95% CI: 0.17 to 0.48) and CAQ cardiac anxiety (β=0.42 95% CI: 0.27 to 0.57).

Table 2: Univariable Linear regression with TSK-NL Heart as dependent variable (N=149)

Variable	Standardized Beta (95% CI)	Adjusted R-square	P-value
Demographics			
Age (continuous)	-0.13 (-0.29 to 0.04)	0.001	0.13
Age ≤ 50	0.22 (0.38 to 2.49)	0.05	0.008
Female Sex	0.19 (0.03 to 0.35)	0.03	0.02
Higher Education	-0.24 (-0.40 to -0.08)	0.05	0.003
Index event			
Acute coronary syndrome	0.08 (-0.08 to 0.25)	0.001	0.31
Stable angina revascularization	-0.04 (-0.21 to 0.12)	-0.001	0.61
Atrial Fibrillation	-0.04 (-0.21 to 0.12)	-0.001	0.59
Admission			
Acute admission	0.07 (-0.09 to 0.24)	0.001	0.37
Treatment index event			
PCI	0.02 (-0.14 to 0.19)	-0.01	0.79
ECV	-0.02 (-0.19 to 0.14)	-0.01	0.99
Medication only	-0.01 (-0.16 to 0.16)	-0.01	0.99
Cardiac disease history			
Acute coronary syndrome	-0.08 (-0.25 to 0.08)	0.001	0.32
PCI	0.001 (-0.16 to 0.16)	-0.001	0.49
CABG	0.06 (-0.10 to 0.22)	-0.001	0.46
Stroke	-0.11 (-0.28 to 0.49)	0.001	0.17
Peripheral artery disease	0.03 (-0.13 to 0.20)	-0.001	0.40
CVD risk factors			
Diabetes mellitus	-0.02 (-0.18 to 0.15)	-0.001	0.83
History of hypertension	0.03 (-0.13 to 0.20)	-0.01	0.69
History of dyslipidaemia	0.08 (-0.09 to 0.24)	-0.001	0.35
BMI	0.14 (-0.19 to 0.30)	0.01	0.08
Psychological risk factors			
GSES General Self-Efficacy scale	-0.18 (-0.34 to -0.02)	0.03	0.03
HADS Anxiety	0.27 (0.11 to 0.42)	0.06	0.001
HADS Depression	0.32 (0.16 to 0.47)	0.09	0.001
IMSA Biological complexity	0.21 (0.06 to 0.37)	0.04	0.009
IMSA Psychological complexity	0.32 (0.17 to 0.48)	0.10	0.001
IMSA Social complexity	0.33 (0.17 to 0.48)	0.10	0.001
CAQ Cardiac anxiety	0.42 (0.27 to 0.57)	0.17	0.001

GSES: General Self Efficacy Scale, HADS: Hospital Anxiety and Depression Scale, IMSA: InterMed Self-Assessment, CAQ: Cardiac Anxiety Questionnaire

In patients referred for CR (N=82), 9 candidate predictors of CR-initiation were found. TSK Kinesiophobia (OR: 0.92 95% CI: 0.85 to 1.00), treatment with ECV (OR:0.21 95% CI: 0.07 to 0.69), atrial fibrillation (OR: 0.21 95% CI: 0.07 to 0.69), HADS anxiety (OR: 0.89 95% CI: 0.79 to 1.00), HADS depression (OR:0.93 95%CI: 0.81 to 1.06), and IMSA psychological complexity (OR: 0.82 95% CI: 0.66 to 1.00) decreased the odds of CR initiation. Treatment with PCI (OR: 3.56 95% CI: 1.15 to 11:00), acute admission (OR: 2.58 95% CI: 0.89 to 7.54) and GSES Self-efficacy (OR: 1.18 95% CI: 1.03 to 1.36) increased the odds for CR initiation **(table 3).** In those referred for CR, 7 patients were readmitted to the hospital for an unplanned procedure, of which 6 initiated CR (OR: 2.18 95%CI: 0.32 to 2.85). An overview of all candidate predictors of CR in the total sample (N=149) is found in **Supplementary table 2.**

Table 3: Univariable logistic regression with CR initiation as dependent variable in a subsample referred for CR (N=82)

Variable	CR-initiation No (N=21)	CR-initiation Yes (N=61)	OR (95% CI)	P-value
Demographics				
Age	63 (11.0)	63 (19.0)	0.98 (0.94 to 1.01)	0.49
Age ≤ 50	1 (1.2)	12 (14.6)	4.90 (0.60 to 40.22)	0.14
Age >50	20 (24.4)	49 (59.8)	0.20 (0.03 to 1.66)	0.14
Female sex (%)	7 (33.3)	11 (18.0)	0.44 (0.14 to 1.36)	0.14
Higher education (%)	16 (23.9)	19 (31.1)	1.92 (0.57 to 6.46)	0.29
Index event				
Acute coronary syndrome (%)	6 (28.6)	30 (49.2)	2.42 (0.83 to 7.11)	0.11
Stable angina revascularization (%)	7 (33.3)	23 (37.7)	1.21 (0.43 to 3.44)	0.72
Atrial fibrillation (%)	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.68)	0.01
Admission type				
Acute admission index event	6 (4.0)	31 (20.8)	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	1 (4.8)	6 (9.8)	2.18 (0.25 to 19.22)	0.48
Treatment index event				
PCI	13 (61.9)	52 (85.2)	3.56 (1.49 to 16.00)	0.03
ECV	8 (38.1)	7 (11.5)	0.21 (0.07 to 0.69)	0.10
Medication only	-	2 (3.3)	-	-
Cardiac disease history				
Acute coronary syndrome	3 (14.3)	15 (24.6)	1.96 (0.51 to 7.58)	0.33
PCI	9 (42.9)	22 (36.1)	0.75 (0.27 to 2.07)	0.58
CABG	-	4 (6.6)	-	-
Stroke	2 (9.5)	2 (3.3)	0.33 (0.42 to 2.45)	0.27
Peripheral artery disease	1 (4.8)	2 (3.3)	0.68 (0.06 to 7.38)	0.76
CVD risk factors				
Diabetes Mellitus (%)	4 (19.0)	11 (18.0)	0.94 (0.26 to 3.33)	0.92
Hypertension (%)	8 (38.1)	23 (37.7)	0.98 (0.35 to 2.73)	0.98
Dyslipidemia (%)	5 (23.8)	19 (31.1)	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.07 (1.16)	27.02 (1.20)	0.96 (0.78 to 1.18)	0.69
Psychological risk factors				
Median TSK Kinesiophobia (IQR)	29.00 (10.78)	27.93 (7.00)	0.92 (0.85 to 1.00)	0.06
Median GSES Self-Efficacy (IQR)	32.67 (5.50)	33.49(7.00)	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	7.00 (4.00)	5.39(4.99)	0.89 (0.79 to1.00)	0.06
Median HADS Depression (IQR)	5.00 (5.21)	4.00(5.70)	0.93 (0.81 to1.06)	0.06
Median IMSA Biological complexity	14 (2.63)	15 (4.00)	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.64(4.0)	5.42(2.81)	0.82 (0.66 to1.00)	0.06
Median IMSA Social complexity (IQR)	7.89 (3.50)	8.64 (3.00)	1.02 (0.83 to 1.27)	0.84
Median CAQ Cardiac Anxiety	26.45 (7.00)	27.00 (11.00)	0.97 (0.92 to 1.03)	0.36

Path analysis

Analysis 1: Total sample

In the total sample we identified three variables that were associated with kinesiophobia **(table 4).** CAQ cardiac anxiety (β = 0.33 95% CI: 0.19 to 0.48) was moderately associated with kinesiophobia. A small association was found between kinesiophobia and IMSA social complexity (β = 0.23 95% CI: 0.06 to 0.39) and higher education (β = -0.18 95% CI: -0.34 to -0.02). We identified two predictors of CR-initiation: age (years) (OR: 0.96 95% CI: 0.93 to 0.99) decreased, while higher levels of GSES self-efficacy (OR: 1.10 95% CI: 1.01 to 1.20) increased the odds for CR-initiation. An overview of all variables associated with kinesiophobia and CR-initiation are presented in a path analysis diagram **(figure 4).**

Model fit (X^2= -2.254124, DF: 5 , P > 0.9).

fig4:pathmodeltotal

Table 4: Path analysis with TSK and CR as dependent variables (N=149)

Dependent variable: TSK		
Variable	**Standardized Beta (95% CI)**	**P-value**
CAQ Cardiac anxiety	0.33 (0.19 to 0.48)	0.001
IMSA Social complexity	0.23 (0.06 to 0.39)	0.006
Higher Education	-0.18 (-0.34 to -0.02)	0.03
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
Age	0.96 (0.93 to 0.99)	0.02
GSES Self-Efficacy	1.10 (1.01 to 1.20)	0.03

Analysis 2: Subsample referred for CR

In the subsample that was referred for CR, we identified two variables that were associated with kinesiophobia **(table 5).** A moderate positive association was found between CAQ cardiac anxiety (β = 0.43 95% CI: 0.24 to 0.62) and kinesiophobia, while GSES self-efficacy (β=-0.29 95% CI: -0.47 to -0.12) was negatively associated with kinesiophobia. Age (OR= 0.98 95% CI: 0.94 to 1.02) was kept in the model since model fit decreased after omission of this variable and age <50 was significantly associated with kinesiophobia and initiation of CR **(table 2)** and **(Supplementary table 2).** Corrected for age, kinesiophobia (OR=0.92 95% CI: 0.84 to 0.99) significantly decreased the odds of CR-initiation. A moderate indirect effect of CAQ cardiac anxiety (OR = 0.98 95% CI: 0.95 to 1.00) on CR-initiation was found with kinesiophobia as a mediator. The subsample analysis is presented in a path analysis diagram **(figure 5).** Model fit (X^2= -0.0062, DF: 4, P > 0.99).

fig5:pathmodelsubsample

Table 5: Path analysis with TSK and CR- initiation as dependent variables, restricted to patients who had been referred to CR (N=82)

Dependent variable: TSK		
Variable	**Standardized Beta (95%CI)**	**P-value**
CAQ Cardiac anxiety	0.43 (0.24 to 0.62)	0.001
GSES Self-Efficacy	-0.29 (-0.47 to -0.12)	0.001
Dependent variable: CR-initiation		
Variable	**OR (95%CI)**	**P-value**
TSK Kinesiophobia		
Model a	0.92 (0.85 to 0.99)	0.05
Model b	0.92 (0.84 to 0.99)	0.04
Model c	0.93 (0.86 to 1.01)	0.08
Model c+d	0.92 (0.85 to 1.01)	0.07
Mediation analysis: indirect effect of cardiac anxiety an self-efficacy on CR-initiation with TSK as mediator		
Variable	**OR (95%CI)**	**P-value**
CAQ Cardiac Anxiety	0.98 (0.95 to 1.00)	0.05
GSES Self-efficacy	1.04 (0.99 to 1.09)	0.11

a = Crude association b = Corrected for age, c = Corrected for gender, d = Corrected for age + gender

DISCUSSION

We found that mild and moderate levels of kinesiophobia were present at hospital discharge in a substantial group of patients with CVD (53% and 22.1% respectively). Cardiac anxiety, social complexity, and educational level were associated with kinesiophobia at hospital discharge. In patients who were referred for CR, self-efficacy was negatively associated with kinesiophobia. In patients referred for CR, the presence of kinesiophobia was associated with a lower rate of CR initiation. An indirect effect of cardiac anxiety on CR-initiation was found.

Our study shows that kinesiophobia decreases the likelihood of CR initiation. Theoretically this makes sense since the construct kinesiophobia comprises `fear of injury', `perception of risk' and `avoidance of physical activity'. Patients with higher levels of kinesiophobia might associate participation in CR as threatening since exercise and physical activity are the cornerstones of CR.

We identified a moderate association between cardiac anxiety and kinesiophobia. In a previous study a similar result was found [1]. Moreover, we found that kinesiophobia mediated the relationship between cardiac anxiety and CR-initiation. This finding is in line with previous research which reports that kinesiophobia mediates the relationship between self-rated anxiety and CR-attendance [4]. The CAQ measures behaviour and anxiety-related symptoms (e.g. *"I avoid activities that make my heart beat faster"*) whereas the TSK-NL Heart measures patients' beliefs about their physical state (e.g. *"If I tried to be physically active my heart problem would increase"*). More research is needed to investigate the impact of specific kinesiophobic beliefs on behaviour and anxiety related symptoms and vice versa.

In line with our findings, Brunetti et al, showed that educational level was negatively associated with kinesiophobia [16]. In a previous study, we found that patients with high levels of kinesiophobia often do not understand medical information and misinterpret body signals, which in turn is associated with poor health literacy and low educational level [3][17].

This finding fits well with the call for more tailored and understandable information at hospital discharge, provided by a trained healthcare provider [3].

Patients scoring high on social complexity suffered from higher levels of kinesiophobia. This is in line with our previous study where we found that patients with lower levels of kinesiophobia often experienced greater social support than those with higher levels of kinesiophobia [3]. The presence of a partner has been shown to improve lifestyle modification in cardiac patients and increase adherence to CR [18]. Moreover, participation of partners in CR-programs improves PA-levels in patients [19][20]. Future studies should evaluate the role of social support on levels of kinesiophobia after cardiac hospitalization.

Self-efficacy was negatively associated with kinesiophobia, in those referred for CR, and predicted CR-initiation in the total sample. Self-efficacy refers to `one's belief in their capacity to execute behaviours necessary to produce specific performance attainments' [21]. The association between self-efficacy and kinesiophobia has been shown in patients with musculoskeletal disorders, but not in patients with CVD [22][23]. Zelle et al., reported that the impact of kinesiophobia on physical activity is largely mediated by self-efficacy, and should therefore be evaluated when targeting kinesiophobia [24]. Our study showed that self-efficacy increased the likelihood of CR-initiation by 10%. Self-efficacy is linked to CR-initiation, but is often lacking in patients with psychological distress [25]. Therefore, self-efficacy-building activities should be considered *before* CR-initiation [26]. Currently, behaviour change strategies are offered in CR-programs to improve PA levels, promote smoking cessation and a healthy diet [27]. However, these interventions are currently limited to those that initiate CR. An early behavioural intervention, aimed at reducing kinesiophobia and stimulating self-efficacy shorty after hospital discharge might improve CR-initiation.

Strengths and limitations

Our study has several strengths. First, we studied kinesiophobia and CR-initiation using a prospective design. We were therefore able to study the temporal sequence of kinesiophobia

and CR-initiation, and multiple factors that impacted our outcomes. Second, using a path model allows for the specification of multiple, dependent and independent variables simultaneously and thereby gives insight into complex relationships between variables [12]. Our comprehensive path analysis gives insight in the factors that are associated with kinesiophobia and predict CR-initiation. These findings aid the development of tailored interventions to target kinesiophobia and improve CR-initiation.

Our study has some limitations. First, a substantial number of patients were included after the start of the COVID-19 pandemic. Although CR was offered remotely, this might have impacted kinesiophobia levels and CR-initiation. Second, by using path analysis we were able to explore a network of sequential relations with contributions from all paths (direct and indirect). Conceptually, a mediation model (in contrast to a confounding model) assumes that a series of variables relate via a causal chain of effect and each variable in the model affects variables occurring later in the chain [28]. In our model, an indirect effect of cardiac anxiety, through kinesiophobia, was found on CR-initiation. Theoretically, our finding makes sense, since somatic symptoms such as chest pain or palpitations (cardiac anxiety), can lead to negative beliefs about one's physical state (kinesiophobia), which in turn might lead to not initiating CR. Future studies should evaluate the potential mediating role of kinesiophobia in the uptake of CR. Third, although our interest is in causes of kinesiophobia and kinesiophobia as a cause of not initiating CR, our observational study does not permit any claims with regard to causal inference since necessary conditions for causal inference (exchangeability, positivity and consistency) have most likely not been met [29]. Nevertheless, this study reports important associations between baseline variables and kinesiophobia. In addition, we showed that kinesiophobia decreased the likelihood of CR-initiation. Future studies, using a causal design can use these results to investigate determinants of kinesiophobia and the effect of kinesiophobia on CR-initiation.

CONCLUSION

Kinesiophobia is prevalent at hospital discharge. Path analysis revealed that cardiac anxiety

and social complexity were positively associated, whereas educational level, and self-efficacy were negatively associated with kinesiophobia at hospital discharge. In addition, patients with (high levels of) kinesiophobia were less likely to initiate CR.

Figure Legends

Figure 1: Hypothetical path model

Figure 2: Flowchart of study

Figure 3: Kinesiophobia scores at hospital discharge

Figure 4: Path analysis in total sample (N=149)

Figure 5: Path analysis in subsample referred for CR

Acknowledgement:

The authors are grateful to department of Cardiology of the Amsterdam University Medical Centre, all research nurses involved in the data collection and patients who participated in this study: Hiltje van der Werf, Manon Ootes, Marjon van Maarl and Willeke Veenhuizen.

Contributors:

GR, BV, HTJ, CHM and WSoR participated in the design of the study. PK and ICDvD were responsible for coordination and acquisition of the data. PK, KK and GR performed the statistical analysis. All authors contributed to the preparation, critical review and approved the final manuscript.

Funding:

Financial support was received from the Dutch Research Council (NWO) as a personal grant (PK; nr: 023.010.064) and a RAAK-PRO grant (RAAK.PRO02.083).

The funding bodies had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Data availability statement

Data are available on reasonable request. Requests for analyses of data from this study should be directed to: P Keessen (p.keessen@hva.nl).

Ethics statements

Patient consent for publication

Not required.

Ethics approval

The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study (protocol number: NL65218.018.18).

Conflict of interest

We have read and understood BMJ policy on declaration of interests and declare that we have no conflicting interests.

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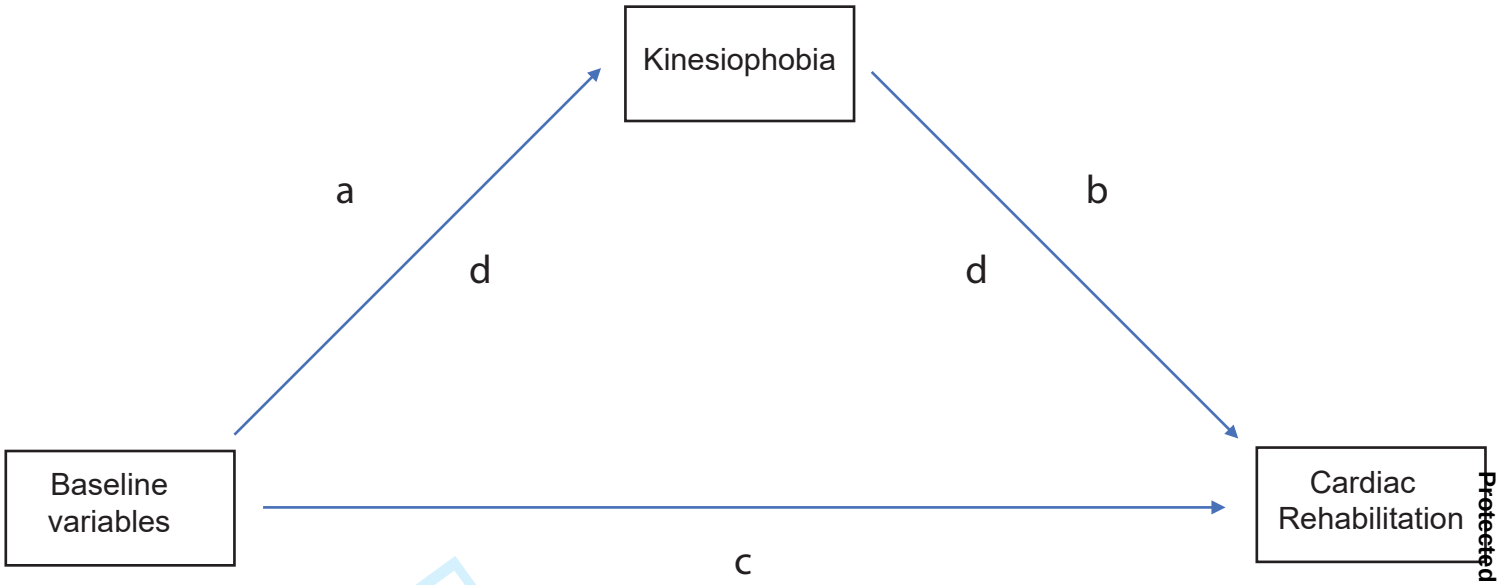


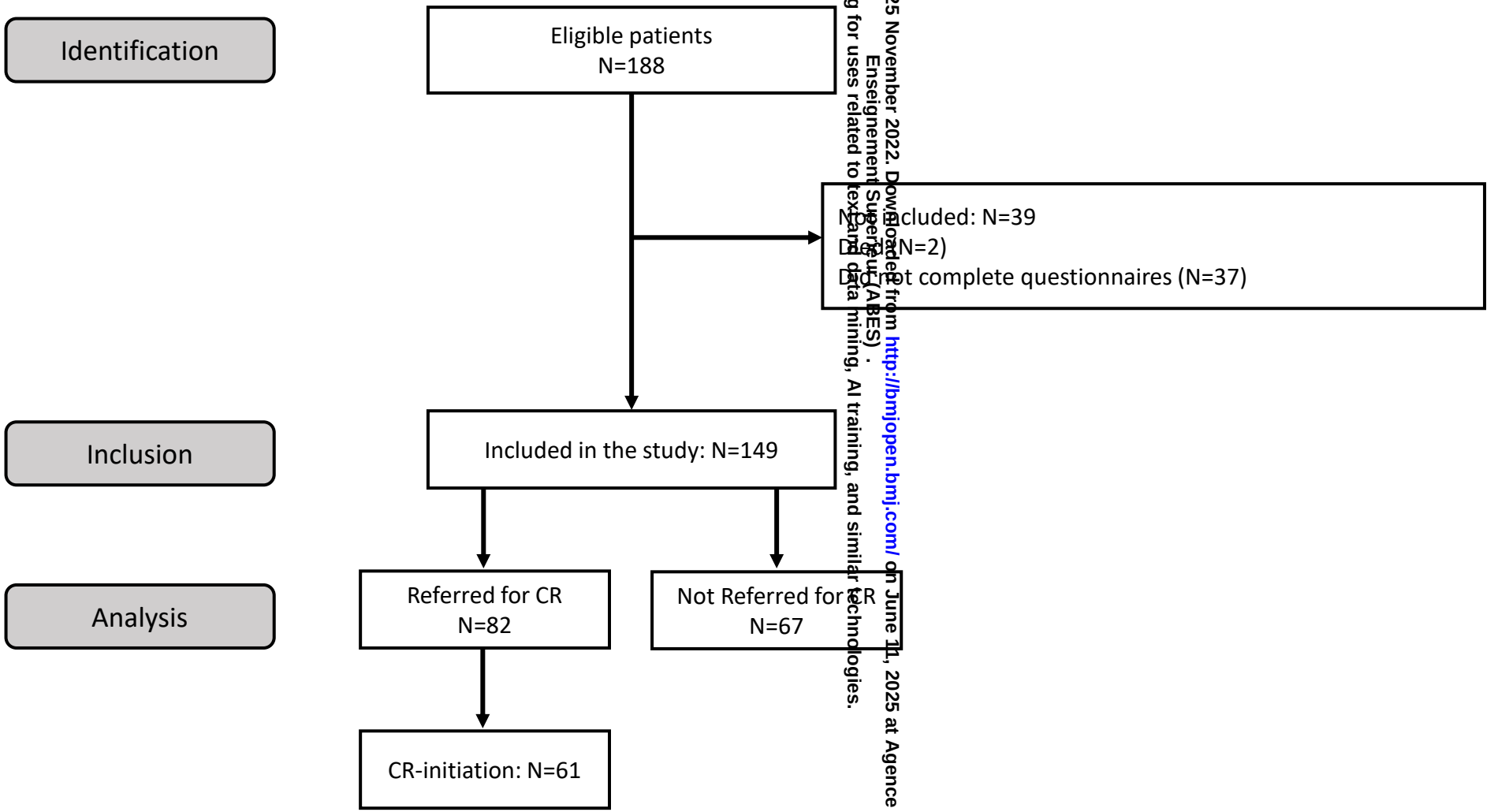
Analyses

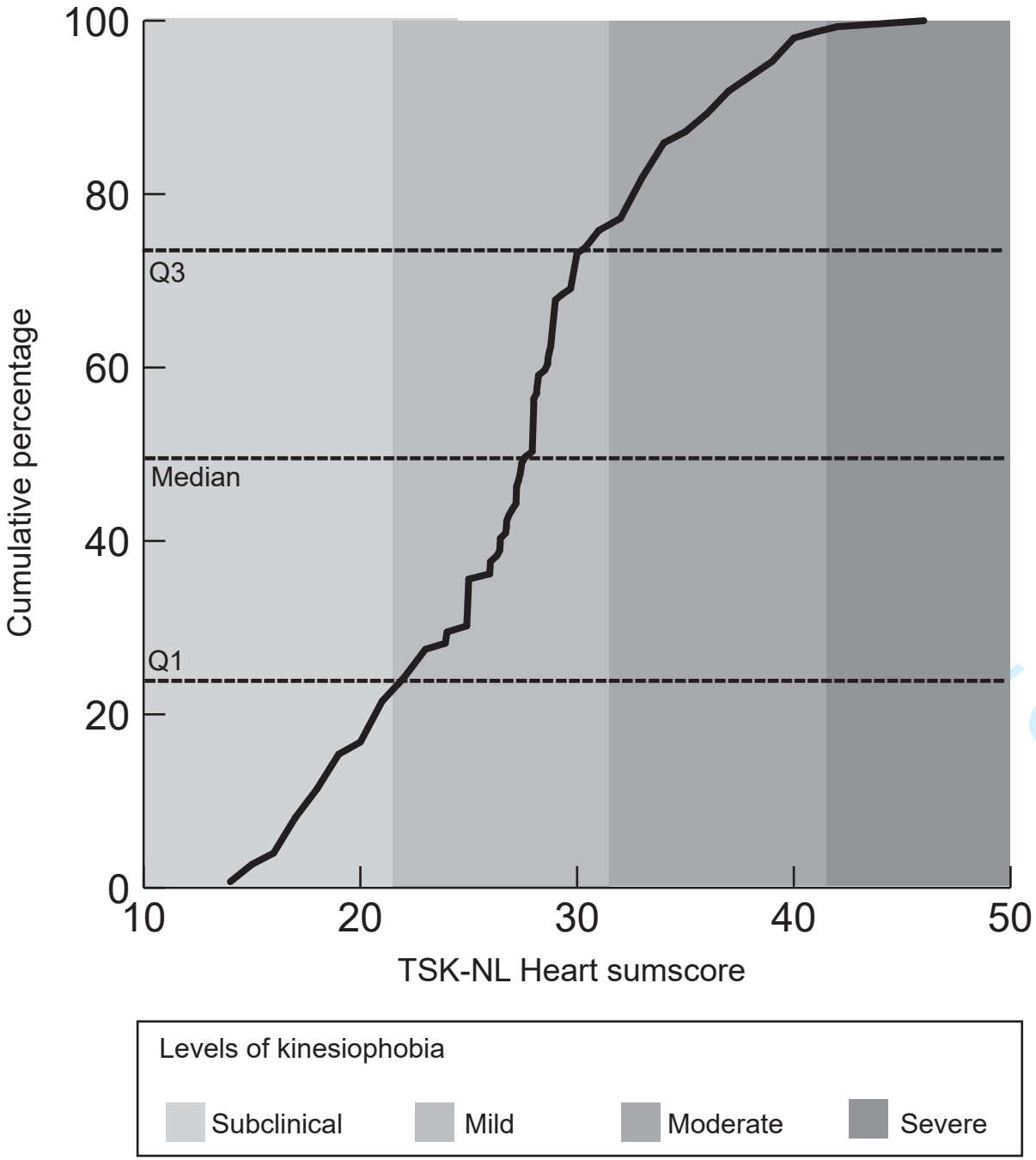
a. Direct effect of baseline variables on kinesiophobia.

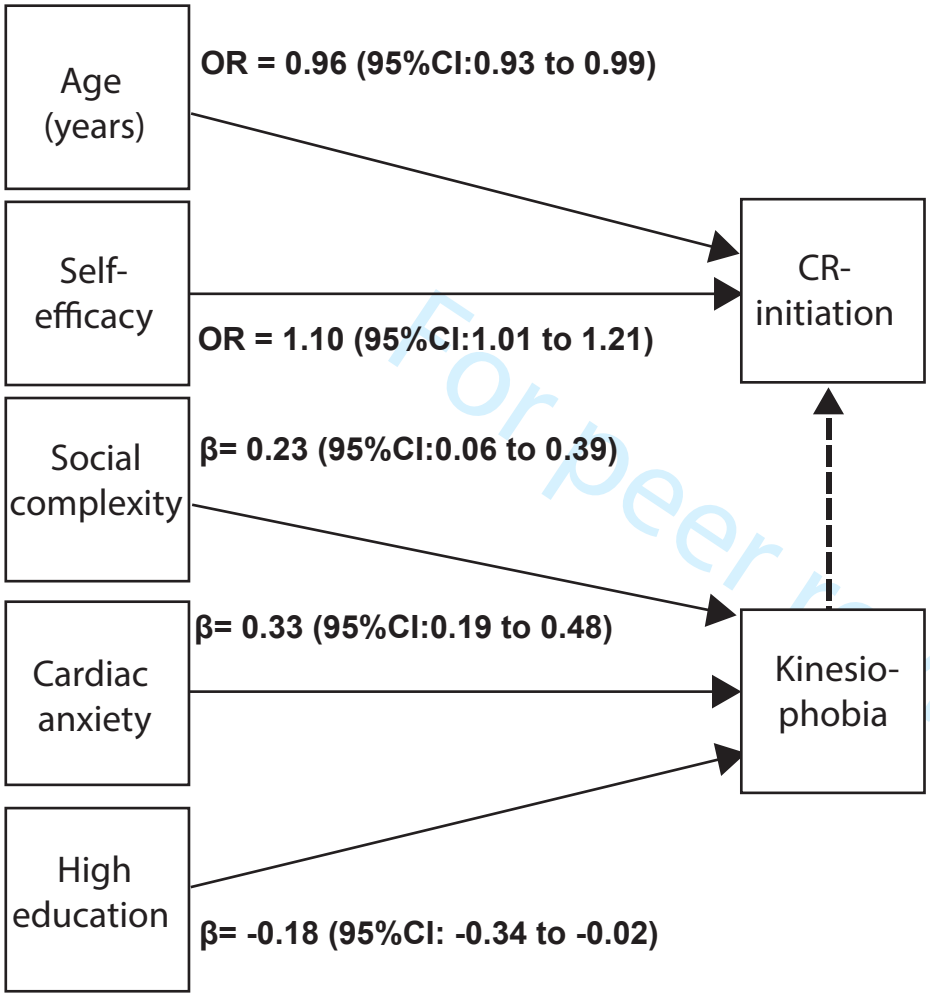
b. Direct effect of kinesiophobia on CR-initiation.

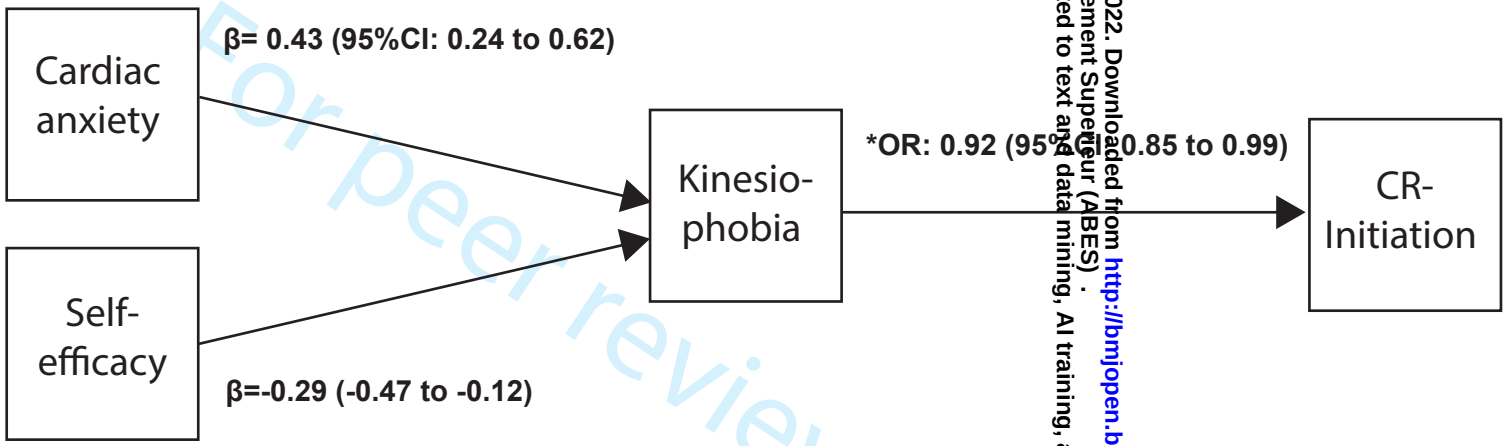
c. Direct effect of baseline variables on CR-initiation.

d. Indirect effect of baseline variables on CR-initiation, with kinesiophobia as mediator.









Supplementary Table 1: Statistical Analysis

Variable	Data type	Missing data (%)	Regressed on outcome: 1. TSK NL- Heart 2. CR initiation
Demographics			
Age	Continuous	-	1+2
Female Sex	Binary	-	1+2
Higher Education	Binary	-	1+2
Index event			
Acute coronary syndrome	Binary	-	1+2
Stable angina revascularization	Binary	-	1+2
Atrial Fibrillation	Binary	-	1+2
Admission			
Acute admission	Binary	-	1+2
Treatment index event			1+2
PCI	Binary	-	1+2
ECV	Binary	-	1+2
Medication only	Binary	-	1+2
Cardiac disease history			
Acute coronary syndrome	Binary	-	1+2
PCI	Binary	-	1+2
CABG	Binary	-	1+2
Stroke	Binary	-	1+2
Peripheral artery disease	Binary	-	1+2
CVD risk factors			
Diabetes mellitus	Binary	-	1+2
History of hypertension	Binary	-	1+2
History of dyslipidaemia	Binary	-	1+2
BMI	Continuous	-	1+2
Psychological risk factors			
GSES General Self-Efficacy scale	Continuous	26 (17.4)	1+2
HADS Anxiety	Continuous	26 (17.4)	1+2
HADS Depression	Continuous	26 (17.4)	1+2
IMSA Biological complexity	Continuous	28 (18.8)	1+2
IMSA Psychological complexity	Continuous	28 (18.8)	1+2
IMSA Social complexity	Continuous	28 (18.8)	1+2

CAQ Cardiac anxiety	Continuous	25 (16.8)	1+2
Outcomes variables			
Cardiac rehabilitation initiation	Binary	-	-
TSK Tampa Scale for Kinesiophobia	Continuous	34 (22.8)	2

Missing data analyses

This study was part of a large project where data were collected at 4 timepoints (hospital discharge, 3 weeks, 6 weeks and 12 weeks). Patients were included in the analyses if they completed the TSK-Heart NL questionnaire on, at least, one of the aforementioned timepoints. In total, 149 patients were included in the analyses. Missing values of the TSK-NL Heart were: Hospital discharge: 34 (22.8%), 3 weeks: 37 (24.8%), 6 weeks: 42 (28.2%), 12 weeks: 54 (36.2%). Little's MCAR test was used to determine patterns of missing data. (Little's MCAR Test Chi Square = 4871,310 DF= 4995, Sig =0.893). A full conditional model (FCS MI) was used to impute data in m=5 datasets. FCS MI is a powerful method to create multiple imputations in datasets with categorical and continuous variables and is well suited for datasets with complex structures [1].

1. Liu Y, De A. Multiple Imputation by Fully Conditional Specification for Dealing with Missing Data in a Large Epidemiologic Study. Int J Stat Med Res. 2015;4(3):287-295. doi: 10.6000/1929-6029.2015.04.03.7. Epub 2015 Aug 19. PMID: 27429686; PMCID: PMC4945131.

Supplementary Table 2: Univariable logistic regression analysis with CR initiation in the Total sample and subsample referred for CR

	Total Sample (N=149)				Referred for CR (N= 82)	
Variable	CR-initiation No (N=88)	CR-initiation Yes (N=61)	OR (95%CI)	P-value*	OR (95%CI)	P-value*
Demographics						
Median age	66(48.0)	63(19.0)	0.96 (0.93 to 0.99)	0.02	0.98 (0.94 to 1.03)	0.49
Female sex (%)	21 (14.1)	11 (7.4)	0.70 (0.31 to 1.59)	0.40	0.44 (0.14 to 1.35)	0.15
Higher education (%)	68 (45.6)	42 (28.2)	0.65 (0.31 to 1.36)	0.25	0.52 (0.15 to 1.76)	0.29
Index event						
Acute coronary syndrome (%)	33 (22.1)	30 (20.1)	1.61 (0.83 to 3.13)	0.16	2.42 (0.83 to 7.07)	0.11
Stable angina revascularization (%)	35 (23.5)	23 (15.5)	0.92 (0.47 to 1.79)	0.8x	1.21 (0.43 to 3.22)	0.72
Atrial Fibrillation (%)	18 (12.1)	7 (4.7)	0.50 (0.20 to 1.29)	0.15	0.21 (0.07 to 0.69)	0.01
Admission type						
Acute admission (%)	35 (23.5)	31(20.8)	1.56 (0.81 to 3.02)	0.18	2.58 (0.89 to 7.54)	0.08
Unplanned admission during study (%)	9 (6.0)	6 (4.0)	0.96 (0.32 to 2.85)	0.94	2.18 (0.25 to 19.26)	0.48
Treatment index event						
PCI (%)	65 (43.6)	52 (34.9)	2.04 (0.87 to 4.80)	0.10	3.56 (1.15 to 11.0)	0.03
ECV (%)	17 (11.4)	7 (4.7)	0.54 (0.21 to 1.40)	0.21	0.21 (0.07 to 0.69)	0.10
Medication only (%)	6 (4.0)	2 (1.3)	0.46 (0.09 to 2.38)	0.36	-	-
Cardiac disease history						
Acute coronary syndrome (%)	20 (13.5)	15 (10.1)	1.09 (0.51 to 2.35)	0.82	1.96 (0.51 to 7.58)	0.33
PCI (%)	34 (22.8)	22 (14.8)	0.90 (0.46 to 1.76)	0.75	0.75 (0.27 to 2.07)	0.58
CABG (%)	1 (0.7)	4 (2.7)	6.11 (0.67 to 56.02)	0.11	-	-
Stroke (%)	12 (8.1)	2 (1.3)	0.22 (0.05 to 0.99)	0.05	0.32 (0.04 to 2.45)	0.27
Peripheral artery disease (%)	8 (5.4)	2 (1.3)	0.34 (0.07 to 1.66)	0.18	0.68 (0.06 to 7.88)	0.76
CVD risk factors						
Diabetes Mellitus (%)	15 (10.1)	11 (7.4)	1.07 (0.45 to 2.52)	0.88	0.94 (0.26 to 3.33)	0.92
History of hypertension (%)	38 (25.5)	23 (15.4)	0.80 (0.41 to 1.55)	0.50	0.98 (0.35 to 2.73)	0.98
History of dyslipidemia (%)	20 (13.4)	19 (12.8)	1.54 (0.74 to 3.21)	0.25	1.45 (0.46 to 4.53)	0.53
Median BMI, kg/m^2 (IQR)	27.28 (1.42)	27.03 (1.20)	1.01 (0.88 to 1.15)	0.91	0.96 (0.78 to 1.18)	0.69
Psychological risk factors						
Median TSK Kinesiophobia (IQR)	27.73 (10.50)	27.93 (93)	0.99 (0.95 to 1.05)	0.93	0.92 (0.85 to 1.00)	0.06
Median GSES Self Efficacy (IQR)	32.86 (4.84)	33.49 (7.00)	1.11 (1.01 to 1.21)	0.02	1.18 (1.03 to1.36)	0.02
Median HADS Anxiety (IQR)	4.29 (4.17)	5.39 (4.99)	0.92 (0.84 to 1.00)	0.06	0.89 (0.79 to 1.00)	0.06
Median HADS Depression	4.65 (4.32)	4.00 (5.70)	0.96 (0.87 to 1.06)	0.44	0.93 (0.81 to 1.06)	0.27
Median IMSA Biological complexity	14.27 (3.00)	15.00 (4.00)	0.99 (0.90 to 1.09)	0.92	1.02 (0.88 to 1.18)	0.84
Median IMSA Psychological complexity	6.00 (3.07)	5.42 (2.81)	0.87 (0.74 to 1.02)	0.09	0.82 (0.66 to 1.00)	0.06
Median IMSA Social complexity	7.79 (3.00)	8.64 (3.00)	1.08 (0.93 to 1.24)	0.32	1.02 (0.83 to 1.27)	0.84
CAQ Cardiac anxiety	26 (10.50)	27 (11.00)	0.99 (0.95 to 1.02)	0.44	0.97 (0.91 to 1.03)	0.36

In the total sample (N = 149) univariable logistic regression analyses revealed 6 candidate predictors of CR-initiation: Age (OR: 0.96 95% CI: 0.93 to 0.99), HADS anxiety (OR: 0.92 95% CI: 0.84 to 1.00) and IMSA psychological vulnerability (OR: 0.88 95% CI: 0.74 to 1.02) decreased the odds of CR-initiation. Treatment with PCI (OR: 2.04 95% CI: 0.87 to 4.80) and GSES Self-efficacy (OR: 1.11 95% CI: 1.01 to 1.21) increased the odds of CR-initiation.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1 +2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	7-8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	11-18

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11-18
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	17
Discussion			
Key results	18	Summarise key results with reference to study objectives	19-20
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20-21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	21
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.