



The association between self-reported health status and adverse events: a comparison among coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI)

Stine Nørris Nielsen^{1,2} · Trine Bernholdt Rasmussen³ · Jens Flensted Lassen^{1,2} · Selina Kikkenborg Berg^{4,5} · Lars Thyroee^{1,2} · Jacob Eifer Møller^{1,2} · Lisette Okkels Jensen^{1,2} · Anne Langhoff Thuesen⁶ · Anne Vinggaard Christensen⁴ · Ola Ekholm⁷ · Rikke Mols⁸ · Charlotte Brun Thorup⁹ · Britt Borregaard^{1,2,6}

Accepted: 30 June 2020 / Published online: 28 August 2020
© Springer Nature Switzerland AG 2020

Abstract

Purpose While several studies have investigated clinical outcomes following coronary artery bypass grafting (CABG) vs. percutaneous coronary intervention (PCI), studies investigating self-reported health and the association with adverse outcomes are limited. Thus, the aim was to investigate differences in health-related quality of life (HRQoL), anxiety and depression at discharge and the association with a composite endpoint of the first event of acute cardiac readmission, revascularisation or 1-year mortality among patients undergoing CABG vs. PCI.

Methods Data from the national cohort study, DenHeart, were used, including measures of HRQoL; EuroQoL-5D-5L (EQ-5D Index Score and VAS) and HeartQoL (Global, Physical and Emotional), anxiety and depression (Hospital Anxiety and Depression Scale, HADS) and register-based follow-up. A total of 7000 patients were included (CABG $n = 652$, PCI $n = 6348$) (median age 65, 75% men). Cox Proportional Hazard models were performed among a propensity-matched population of responders ($n = 520$).

Results HRQoL was significantly better among patients undergoing PCI vs. CABG, but with no differences in time to readmission or revascularisation. HRQoL, anxiety and depression were significantly associated with the risk of the composite endpoint among the PCI group (Hazard Ratio, HR (95% confidence intervals, CI) [EQ-5D index score 3.07 (1.67–5.67), EQ-5D VAS 0.97 (0.96–0.99), HeartQoL Global 0.61 (0.38–0.95), HeartQoL Emotional 0.56 (0.39–0.80), HADS-D ≥ 8 3.12 (1.61–6.01), HADS-A ≥ 8 2.08 (1.14–3.80)].

Conclusion Patients undergoing PCI reported better HRQoL at discharge compared with patients undergoing CABG, whereas readmission rates were similar. Self-reported health was associated with the risk of adverse events among patients undergoing PCI, but not among patients undergoing CABG.

Clinical trial registration NCT01926145.

Keywords Coronary artery bypass grafting · Percutaneous coronary intervention · Quality of life · Anxiety · Depression · Cardiac readmission

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s11136-020-02573-8>) contains supplementary material, which is available to authorized users.

✉ Stine Nørris Nielsen
stine.noerris.nielsen@hotmail.dk

Extended author information available on the last page of the article

Introduction

Coronary artery disease (CAD) remains the most common cardiovascular disease, and despite improvements in treatment and increased survival, it is still associated with significant morbidity and mortality [1]. A cornerstone in the treatment of CAD includes medical treatment and revascularisation with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) [2]. Both procedures are indicated for relief of symptoms and prolongation of life among patients with ischemic heart disease

[2, 3]. The choice of treatment depends on the severity of symptoms, anatomical complexity, comorbidities, surgical risk–benefit ratio and patient preferences [2]. In acute coronary syndrome and among patients with stable coronary disease, PCI is the most frequently used revascularisation strategy [4], while CABG is particularly beneficial among patients with complex diseases and comorbidities [3]. When comparing outcomes following CABG vs. PCI, a recent propensity-matched observational study demonstrated lower 5-year mortality and lower readmission rates in favour of the CABG population [5]. Similar findings have been demonstrated in randomised trials; the NOBLE, EXCEL and the SYNTAX study, indicating either no difference or lower mortality and/or revascularisation rates after CABG, compared to PCI [6–8].

Revascularisation is performed to improve survival, symptoms and quality of life [2]. However, when investigating differences in self-reported health status, including health-related quality of life (HRQoL) after CABG vs. PCI, current results differ [9–13]. In a short-term perspective (1-month post-procedure), several studies indicate that HRQoL is significantly better among patients undergoing PCI compared to CABG [9, 11–13]. Contrary, on the long term (3–5 years post procedure), studies have demonstrated similar scores of HRQoL among the two groups [9, 10, 12], whereas others again have found a significantly better HRQoL among the CABG group compared to the PCI group [11, 13]. Consistent results are lacking.

The association between HRQoL, anxiety and depression, and outcomes after either CABG or PCI have been investigated in several studies, separately [14–21]. Among patients undergoing CABG, previous studies have suggested an association between symptoms of anxiety, depression and all-cause mortality [14–16]. Similarly, among patients undergoing PCI, symptoms of anxiety or depression have shown to be associated with readmission, revascularisation and mortality rates, [17–21] yet, no studies have compared the associations between worse HRQoL, symptoms of anxiety and depression and the risk of readmission, revascularisations and mortality among patients undergoing CABG vs. PCI in one combined study. Identifying and addressing health issues reported by patients may be valuable in risk management, as patient-reported outcomes are known to reliably be associated with adverse outcomes. Thus, the main objective in patients undergoing CABG vs. PCI was to investigate the association between HRQoL, anxiety and depression and adverse events within 1 year after discharge. Adverse events were defined as a composite endpoint of the first event of acute cardiac readmission, revascularisation or mortality within 1 year.

Methods

Study design

The current study was a sub-study based on data from the DenHeart study. The design of the DenHeart study is described in detail elsewhere [22]. In brief, the DenHeart study is a national cross-sectional cohort study, including a survey with patient-reported outcomes measured at discharge and combined with register-based clinical and socio-demographic variables and register-based follow-up. The overall aim of the DenHeart study was to investigate self-reported health status, including HRQoL, symptom burden, anxiety and depression, and the associations with adverse outcomes in general.

Setting and participants

All patients discharged or transferred from one of five Danish Heart centres, between April 15, 2013 and April 15, 2014, were consecutively offered participation in the DenHeart study. At hospital discharge (baseline), patients were requested to fill out a questionnaire by the ward nurse. Written consent was collected alongside the questionnaire. Patients who were transferred to a local hospital were encouraged to fill out the questionnaire at final discharge. The survey included different instruments measuring various patient-reported outcomes. In the current study, three instruments were included; two instruments measuring HRQoL and one instrument measuring symptoms of anxiety and symptoms of depression. Patients either returned the questionnaire at discharge or by mail within 3 days after discharge. A prepaid postage envelope was distributed alongside the questionnaire.

In the current study, we included patients based on their surgical or interventional procedure codes (Nordic/NOMESCO Classification of Surgical Procedures) [23]; CABG: KFNA, KFNB, KFNC, KFND, KFNE and PCI: KFNG (KFNG00-KFNG05A).

Patients were excluded if they met one of the following criteria: patients under the age of 18, patients who did not understand Danish or patients without a Danish civil registration number. Patients were also excluded for ethical reasons if they were too severely ill to participate, or unconscious upon transfer to another department.

Data sources

Clinical and socio-demographic data

The following clinical and socio-demographic data were obtained: sex, age, marital status, educational level, type of index procedure, type of hospital stay (acute or planned) and comorbidity in the last 10 years (hypertension, ventricular arrhythmia, arrhythmia, myocardial infarction, diabetes, heart failure, renal disease, chronic obstructive pulmonary disease, prior CABG and prior PCI). The data were obtained from the following Danish registers: The Danish Civil Registration System [24], The Danish National Patient Register (NPR) [25] and The Danish Education Register [26]. ICD-10 codes of comorbidity were obtained from the NPR. To evaluate comorbidity, information from the last 10 years (excluding the index admission) was obtained from the NPR, and a Tu-comorbidity index score was calculated based on the information obtained [27]. The Tu-comorbidity index score includes the following comorbidities: arrhythmia, cardiogenic shock, congestive heart failure, pulmonary oedema, malignancy, diabetes, cerebrovascular diseases, chronic obstructive pulmonary disease, acute and chronic renal failure. The score was calculated for the last 10 years, and all diagnoses were weighted equally.

Outcomes

Readmissions were based on data from the NPR and defined as an unplanned admission occurring more than 24 h after index discharge. Only cardiac readmissions occurring within 1 year were included. Revascularisations (acute, sub-acute and staged procedures performed within the first year) were included based on procedure codes from the NPR (Supplementary Table S1). In addition, 1-year all-cause mortality, including date of death, was obtained from The Danish Civil Registration System.

Patient-reported outcome measures

Self-reported health status was measured with the following patient-reported outcomes measurements: the EuroQol 5 Dimensions 5 Levels Questionnaire (EQ-5D 5L, in the following mentioned as EQ-5D) [28], the HeartQoL [29–31], the Hospital Anxiety and Depression Scale (HADS) [32] and four ancillary questions regarding height, weight, smoking status (ever smoker) and alcohol intake above the national recommendation.

The EQ-5D measures current generic health and provides two scores, an index score and a visual analogue scale (VAS) score. The index score comprises questions covering five-health dimensions: mobility, self-care, usual activities,

pain/discomfort and anxiety/depression. The index score ranges from 0 to 3 and the VAS score from 0 to 100 [28]. Higher scores indicate better health status on both scores. A Cronbach's alpha of 0.73 for EQ-5D index score has been demonstrated in patients with ischemic heart disease [33].

The HeartQoL is a disease-specific 14-item questionnaire, measuring HRQoL in cardiac patients. The instrument has a 4-week recall, meaning that the patients' answers are related to symptoms within the past 4 weeks. The score is divided into a global score and two subscales, a physical and an emotional scale, scoring from 0 to 3 on all scales. A high score is associated with a better HRQoL status [29–31]. Cronbach's alphas of 0.92, 0.91 and 0.87 for the global, physical and emotional subscale scores, respectively, have been shown in patients with stable CAD [34].

HADS is a measure of symptoms of anxiety and depression, with 1-week recall. The scale consists of 14 items, divided into two sub-scores, an anxiety score (HADS-A) and a depression score (HADS-D). The scales are summarised from 0 to 21, with a cut-off score ≥ 8 representing the presence of anxiety (HADS-A ≥ 8) or depression (HADS-D ≥ 8) [32]. A Cronbach's alpha of 0.82 for HADS-A and 0.74 for HADS-D in patients with ischemic heart disease have previously been demonstrated [33]. In the following, symptoms of anxiety and depression measured with HADS will be described as "anxiety" and "depression".

Ethics

The DenHeart study was approved by the Danish Data Protection Agency (2007-58-0015/30-0937) and complies with the principles outlined in the Declaration of Helsinki [35]. The DenHeart study is registered at ClinicalTrials.gov (NCT01926145). According to Danish legislation, this type of study does not require approval from a local ethics committee. Written consent was collected alongside the questionnaire.

Statistical methods

Continuous variables were tested for normality using the Shapiro–Wilks test. No continuous variables were normally distributed, and thus, presented as the median and the interquartile range (IQR, the 25th and the 75th percentile). Differences among groups were compared using a Mann–Whitney *U* test. Categorical variables were expressed as the number of patients and percentages and compared using the χ^2 test or Fisher's exact test if categorical variables only included five or fewer observations.

First, to reduce possible bias from confounding variables and control for selection bias among the two groups (CABG vs. PCI), a propensity score matching was performed, as outlined by Rosenbaum and Rubin [36]. The

propensity matching was performed among the responders, as an optimal nearest-neighbour matched propensity score with a calliper width of 0.00005 SD and a 1:1 matching without replacement. The following variables were included in the model: Sex, age, acute/unplanned index admission, procedure (CABG/PCI), marital status, hypertension, diabetes, renal disease, both procedures during the same index admission, myocardial infarction and being a responder. The variables were chosen based on differences among the unmatched populations, but also variables assumed to be related to outcome [37]. To validate the matching process and group-balance, descriptive statistics were used.

Second, to investigate time to first, unplanned, cardiac readmission (or revascularisation) among the two groups of responders (CABG vs. PCI), the cumulative incidence function was estimated using the Fine and Gray cumulative incidence function (a proper summary statistics for analysing competing risk data) [38]. The cumulative incidence function was based on a univariable proportional hazard model with death as a possible competing risk and visualised with incidence curves [39].

Cox proportional hazard regression models were performed to investigate the association between HRQoL (EQ-5D and HeartQoL), anxiety and depression (HADS-A, HADS-D) and adverse events after discharge among the two groups. Adverse events were defined as a composite endpoint of the first event of acute cardiac readmission, revascularisation or all-cause mortality within 1 year. The models were adjusted for sex, age, COPD, prior PCI and current smoking status. Results are presented as hazard ratios (HR) with 95% confidence intervals (CI). Due to a small sample size, and thus, limited possibilities of including all potential confounders, the models were performed with different adjustments as sensitivity analyses. In the sensitivity analyses, prior CABG and arrhythmia were included as potential confounders.

The *p* value was set at a 5% significance level. The analyses were performed using STATA 15.1 (StataCorp LLC, Texas, USA).

Results

Patients and baseline demographics

During the 1-year study period, 662 and 6630 patients underwent CABG or PCI, respectively. In total, 292 were excluded, resulting in a total population of 7000 patients (CABG *n* = 652 and PCI *n* = 6348), as shown in Fig. 1. Of the total population, 3681 patients completed the questionnaire (response rate of 53%, CABG 49% vs. PCI 53%, *p* = 0.049). Differences among responders and non-responders are shown in Supplementary Table S2. In brief, non-responders

were more often female, less likely to be married and more had COPD and a higher Tu-comorbidity score. Also, in the PCI group, non-responders had a lower level of education and were more likely to be admitted acutely.

Among the total population, the median age was 65 years, 75% were men and 47% were acutely admitted. There were several differences in socio-demographic and clinical characteristics among patients receiving CABG vs. PCI before matching (Table 1).

The propensity-matched population consisted of 520 responders, 260 patients in each group. The propensity matching successfully eliminated most differences in socio-demographic and clinical characteristics, except for prior CABG (CABG < 1% vs. PCI 6%, *p* < 0.001), prior PCI (CABG 15% vs. PCI 22%, *p* = 0.042), arrhythmia (CABG 8% vs. PCI 13%, *p* = 0.032), COPD (CABG 3% vs. PCI 7%, *p* = 0.016) and proportion of daily smokers (CABG 4% vs. PCI 12%, *p* = ≤ 0.001), as shown in Table 1.

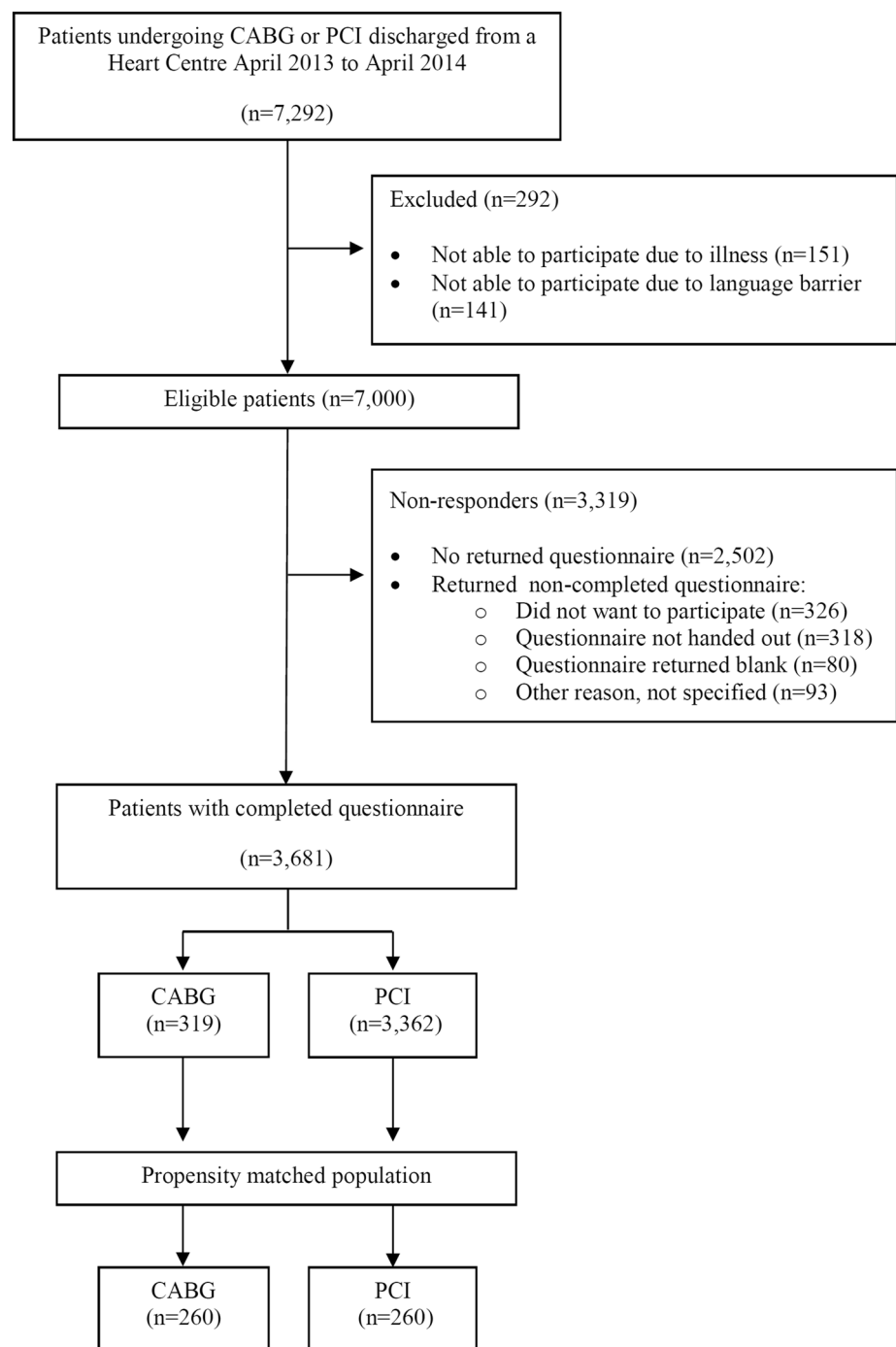
Health-related quality of life, anxiety and depression

Table 2 depicts differences in HRQoL, anxiety and depression among the two groups at discharge. CABG patients were characterised by a lower EQ-5D index score, EQ-5D VAS score, HeartQoL (global, physical and emotional) scores and a lower continuous score of HADS-D compared with the PCI group (Table 2). Also worth highlighting is the seemingly high proportions of patients with anxiety and depression in both groups; 36% of the patients in the CABG group reported anxiety (HADS-A ≥ 8) vs. 33% in the PCI group (*p* = 0.429). Depression (HADS-D ≥ 8) were reported among 22% of the CABG group and 17% of the PCI group (*p* = 0.225) (Table 2). There were no differences in anxiety and depression among groups.

Readmission, mortality and revascularisations

In the propensity-matched population of responders, 23% in the CABG group vs. 19% in the PCI group experienced an acute, cardiac readmission (*p* = 0.332). During follow-up (1 year), less than five patients in the CABG group (< 1%) underwent repeated revascularisation compared vs. 24 patients in the PCI group (9%), *p* < 0.001. In contrast, mortality rates were similar *p* = 0.704 (Table 3). Time to the first event of acute, cardiac readmission or revascularisation with death as a possible competing risk did not differ among groups (*p* = 0.237), as shown in Fig. 2. Data for the total unmatched population are shown in Supplementary Table S3. The two unmatched groups (CABG vs. PCI) were statistically significantly different in planned readmission and revascularisations.

Fig. 1 Patient Flowchart. CABG coronary artery bypass grafting, PCI percutaneous coronary intervention



Health-related quality of life, anxiety and depression, and the risk of adverse events

In the CABG group neither HRQoL, anxiety nor depression were associated with the adverse event in the adjusted analyses. In contrast, patients in the PCI group with depression (HADS-D ≥ 8) had a three-fold higher 1-year risk of experiencing the composite endpoint (HR 3.12, 95% CI 1.61–6.01, $p \leq 0.001$) and a two-fold

increased 1-year risk in those with anxiety (HADS-A ≥ 8) (HR 2.08, 95% CI 1.14–3.80, $p = 0.017$). In addition, among the PCI population, patients reporting scores within the worst quartile of the EQ-5D index score had a higher 1-year risk of the composite endpoint (HR 3.07, 95% CI 1.67–5.67, $p < 0.001$) and better scores of EQ-5D VAS and HeartQoL (global and emotional) reduced the 1-year risk of the composite endpoint (EQ-5D VAS, HR 0.97, 95% CI 0.96–0.99, $p \leq 0.001$, Global, HR 0.61

Table 1 Baseline characteristics among patients undergoing CABG or PCI—the total population and a propensity-matched population

	Total population (<i>n</i> = 7000)		<i>p</i> value	Propensity-matched population (responders) (<i>n</i> = 520)		<i>p</i> value
	CABG (<i>n</i> = 652)	PCI (<i>n</i> = 6348)		CABG (<i>n</i> = 260)	PCI (<i>n</i> = 260)	
Socio-demographic characteristics						
Sex [male, <i>n</i> (%)]	542 (83)	4710 (74)	<0.001	225 (87)	219 (84)	0.456
Age, years (median, IQR)	67 (61–73)	66 (57–74)	<0.001	66 (61–71)	67 (60–72)	0.656
Married, <i>n</i> (%)	426 (65)	3851 (61)	0.020	190 (73)	191 (73)	0.921
Educational level, <i>n</i> (%)*						
Basic school	279 (44)	2698 (44)	0.638	108 (43)	89 (36)	0.215
Upper secondary or vocational School	256 (40)	2336 (38)		108 (43)	113 (45)	
Higher education	101 (16)	1029 (17)		38 (15)	48 (19)	
Clinical characteristics						
Type of hospital stay, <i>n</i> (%)*						
Acute	47 (7)	3222 (52)	<0.001	27 (10)	27 (10)	1.000
Planned	605 (93)	2962 (48)		233 (90)	233 (90)	
Both CABG and PCI during index admission, <i>n</i> (%)	16 (2)	<5	<0.001	–	–	–
Co-morbidity 10 years back, <i>n</i> (%)						
Prior CABG	<5	231 (4)	<0.001	<5	16 (6)	<0.001
Prior PCI	104 (16)	1262 (20)	0.016	39 (15)	57 (22)	0.042
Hypertension	247 (38)	2001 (32)	0.001	84 (32)	93 (36)	0.405
Ventricular arrhythmia	20 (3)	81 (1)	<0.001	<5	<5	1.000
Arrhythmia	73 (11)	740 (12)	0.726	20 (8)	35 (13)	0.032
Myocardial Infarction	224 (34)	1276 (20)	<0.001	63 (24)	49 (19)	0.135
Diabetes	146 (22)	864 (14)	<0.001	36 (14)	50 (19)	0.098
Heart failure	82 (13)	498 (8)	<0.001	21 (8)	23 (9)	0.753
Renal disease	15 (2)	184 (3)	0.382	<5	<5	0.624

Table 1 (continued)

	Total population (<i>n</i> = 7000)		Propensity-matched population (responders) (<i>n</i> = 520)	
	CABG (<i>n</i> = 652)	PCI (<i>n</i> = 6348)	CABG (<i>n</i> = 260)	PCI (<i>n</i> = 260)
Chronic obstructive pulmonary disease	33 (5)	429 (7)	7 (3)	19 (7)
Tu-comorbidity index score				
0	384 (59)	4,000 (63)	181 (70)	160 (62)
1–2	231 (25)	2040 (32)	70 (27)	88 (34)
> 3	37 (6)	308 (5)	9 (3)	12 (5)
Health behaviour, <i>n</i> (%) [‡]				
BMI ≥ 25	224 (75)	2250 (71)	183 (74)	183 (76)
BMI ≥ 30	91 (30)	817 (26)	68 (28)	60 (25)
Current daily smoker	13 (4)	559 (17)	10 (4)	32 (12)
Ever smoker	213 (70)	2424 (74)	180 (73)	193 (75)
Alcohol intake above high-risk limit [‡]	31 (11)	281 (9)	27 (11)	21 (9)

IQR interquartile range, *BMI* body mass index

*Missing data; In total, missing data were present among *n* = 301 (educational data) and *n* = 164 (the type of hospital stay)

[†]Self-reported data-only available among responders of the survey

[‡]The Danish National Board of Health defined the high-risk limit for alcohol consumption as a weekly intake exceeding 21 units for men and 14 units for women at the time point of inclusion

The *p* value was set at a 5% significance level

Table 2 Differences in health-related quality of life, anxiety and depression among patients undergoing CABG vs. PCI in the propensity-matched population

	CABG (<i>n</i> =260)	PCI (<i>n</i> =260)	<i>p</i> value
EQ-5D 5L			
Index score (median, IQR)	0.70 (0.64–0.79)	0.77 (0.70–0.86)	<0.001
VAS score (median, IQR)	70 (55–80)	75 (60–85)	0.005
HeartQoL			
Global score (median, IQR)	1.43 (0.86–2.07)	1.71 (1.14–2.36)	<0.001
Physical subscale score (median, IQR)	1.20 (0.70–2.00)	1.47 (0.90–2.30)	0.002
Emotional subscale score (median, IQR)	2.00 (1.00–2.75)	2.25 (1.75–2.75)	0.004
HADS			
HADS-A (median, IQR)	6 (3–9)	5 (2–8)	0.142
HADS-A ≥ 8 (<i>n</i> , %)	89 (36)	83 (33)	0.429
HADS-A ≥ 11 (<i>n</i> , %)	36 (15)	35 (14)	0.799
HADS-D (median, IQR)	4 (2–7)	3 (1–6)	0.004
HADS-D ≥ 8 (<i>n</i> , %)	54 (22)	44 (17)	0.225
HADS-D ≥ 11 (<i>n</i> , %)	16 (6)	15 (6)	0.817

A higher score indicates a better health status on the EQ-5D and HeartQoL, whereas a higher score on the HADS indicates worse status

EQ-5D The European Quality of Life 5 Dimensions 5 Levels Questionnaire, HADS hospital anxiety and depression scale (HADS-A anxiety, HADS-D depression)

The *p* value was set at a 5% significance level

Table 3 Differences in readmission rates, revascularisations and all-cause mortality within 1 year

Propensity-matched population				
	All (<i>n</i> =520)	CABG (<i>n</i> =260)	PCI (<i>n</i> =260)	<i>p</i> value
All-cause mortality	7 (1)	<5	<5	0.704
All-cause mortality without readmission	<5	<5	<5	1.000
Readmission, cardiac, <i>n</i> (%)				
All (acute and planned)	153 (29)	69 (27)	84 (32)	0.149
Acute	109 (21)	59 (23)	50 (19)	0.332
Planned	44 (8)	10 (4)	34 (13)	<0.001
Revascularisations (acute, sub-acute and staged)	26 (5)	<5	24 (9)	<0.001
Composite event	112 (22)	61 (23)	51 (20)	0.286
Common causes of all readmission, <i>n</i> (% of all/% of readmitted)				
Angina Pectoris, all	38 (7/25)	12 (5/17)	26 (10/31)	0.018
Acute ischemic heart disease*	24 (5/16)	7 (3/10)	17 (7/20)	0.037
Chronic ischemic heart disease	18 (4/12)	7 (4/13)	7 (4/11)	1.000
Other ischemic heart disease	8 (2/5)	<5	<5	1.000
Arrhythmia, all	27 (5/18)	17 (7/25)	10 (4/12)	0.166
Other [†]	38 (7/25)	20 (8/29)	18 (7/21)	0.736

The *p* value was set at a 5% significance level

*ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, acute myocardial infarction, acute myocardial infarction unspecified

[†]Lung embolism, infectious heart disease, heart valve disease, heart failure, congenital heart disease, abdominal aortic aneurism, respiratory failure/dyspnea, vertigo

95% CI 0.38–0.95, *p* = 0.029 and Emotional, HR 0.56, 95% CI 0.39–0.80, *p* = 0.002) as shown in Fig. 3. The crude analyses are shown in Supplementary Table S4. The elements of the composite endpoint were analysed

separately and revealed that the results were driven by the acute readmissions (Supplementary Table S5). Results for the sensitivity analysis are shown in Supplementary Table S6.

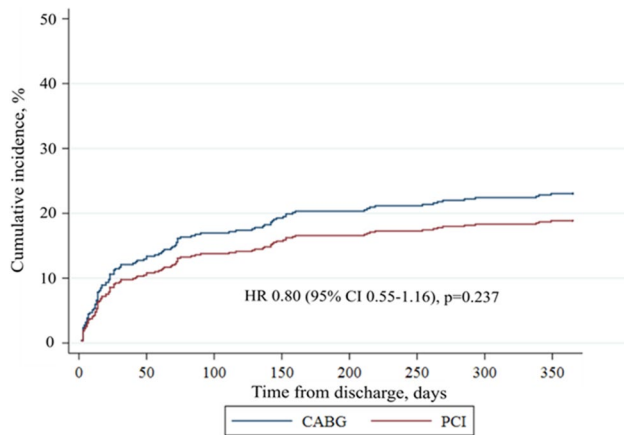


Fig. 2 Cumulative incidence curves showing time to first acute cardiac readmission or revascularisation with death as the possible competing risk (propensity-matched population)

Discussion

In this study, we compared HRQoL, anxiety and depression measured at hospital discharge after either CABG or PCI in a propensity-matched population. We found that patients receiving PCI reported significantly better HRQoL at discharge on most subscales, but with time to readmission or revascularisation being similar. Also, we demonstrated how HRQoL, anxiety and depression among patients undergoing PCI were associated with the risk of experiencing adverse events within 1-year after discharge, whereas no association was found in the CABG group.

Our findings of better HRQoL among patients receiving PCI vs. CABG are in line with previous studies [9, 10, 12, 13], and could possibly be explained by the minimally invasive technique compared to the surgical trauma associated with heart surgery, resulting in immediate mobilisation, fewer restrictions, less pain and a shorter length of stay [6]. Despite mental health being similar among groups, it is still worth highlighting how one-third of all patients report anxiety and one-fifth of all patients report depression. These are seemingly high proportions, indicating the constant importance of post-procedural screening, follow-up and treatment as recommended in guidelines [40]. High scores of anxiety and depression in the first month after PCI have previously been demonstrated in different studies [17, 21], whereas studies and trials investigating interventions aiming at reducing these symptoms are sparse [41, 42].

Although readmission rates were similar among the two groups, one-fifth of the patients experienced an acute cardiac readmission within the first year. Similarly, a recent propensity-matched study demonstrated 1-year readmission rates of 28% in a CABG group vs. 38% in a PCI group [5]; this population, though, was slightly different from ours; a

high-risk multi-vessel coronary artery diseases population, whereas we have included all patients receiving PCI, including patients with a lower risk profile.

When investigating HRQoL, anxiety and depression and the 1-year risk of experiencing adverse events, we found significant associations in the PCI group, but not in the CABG group. As the two groups are seemingly comparable, ensured by the propensity matching and aligned in most known variables, it is likely that the surgical trauma of heart surgery compared with a more minimally invasive approach influences the outcomes differently. When investigating HRQoL, anxiety and depression in different surgical populations, similar results have been found [43, 44]. Contrary, among cardiac patients in general, several studies have demonstrated a significant association between HRQoL, symptoms of anxiety and depression and the risk of adverse outcomes, including mortality [18, 20, 45, 46]. As many complications related to open-heart surgery arise after discharge, the association with adverse outcomes might be challenging to demonstrate. Thus, the use of patient-reported outcomes at discharge might not be an appropriate predictor of future outcomes in populations of patients undergoing cardiac surgery as the surgery itself, the afterwards sternal regime and changed bodily awareness might influence the overall health perception—a concern that has been broached in a previous study [43].

The association between depression and the risk of adverse events complies with results from a recent systematic review and meta-analysis among patients receiving PCI [47], thus, this highlights how depression is a major risk factor for poor outcomes. However, when depression is measured shortly after the PCI, the symptoms could be related to the stress response of the procedure and thereby not a genuine mental disorder [47]; this should be taken into account when interpreting the results. Although most studies, including the current, do not demonstrate a causal relationship between self-reported health status and adverse outcomes (but instead investigate associations between outcomes), it is still important to highlight how poor mental outcomes following the procedures remain a genuine problem. Future prospective studies investigating the causal relationship between depression and worse outcomes following PCI are needed. In addition, our results could potentially be taken into consideration when preparing the patient for discharge. Self-reported health status might be included as a potential screening tool and individualised follow-up regimes might be planned according to the HRQoL and the mental health status of the patient.

Strengths and limitations

The study included a propensity-matched population of patients undergoing either CABG or PCI. The propensity

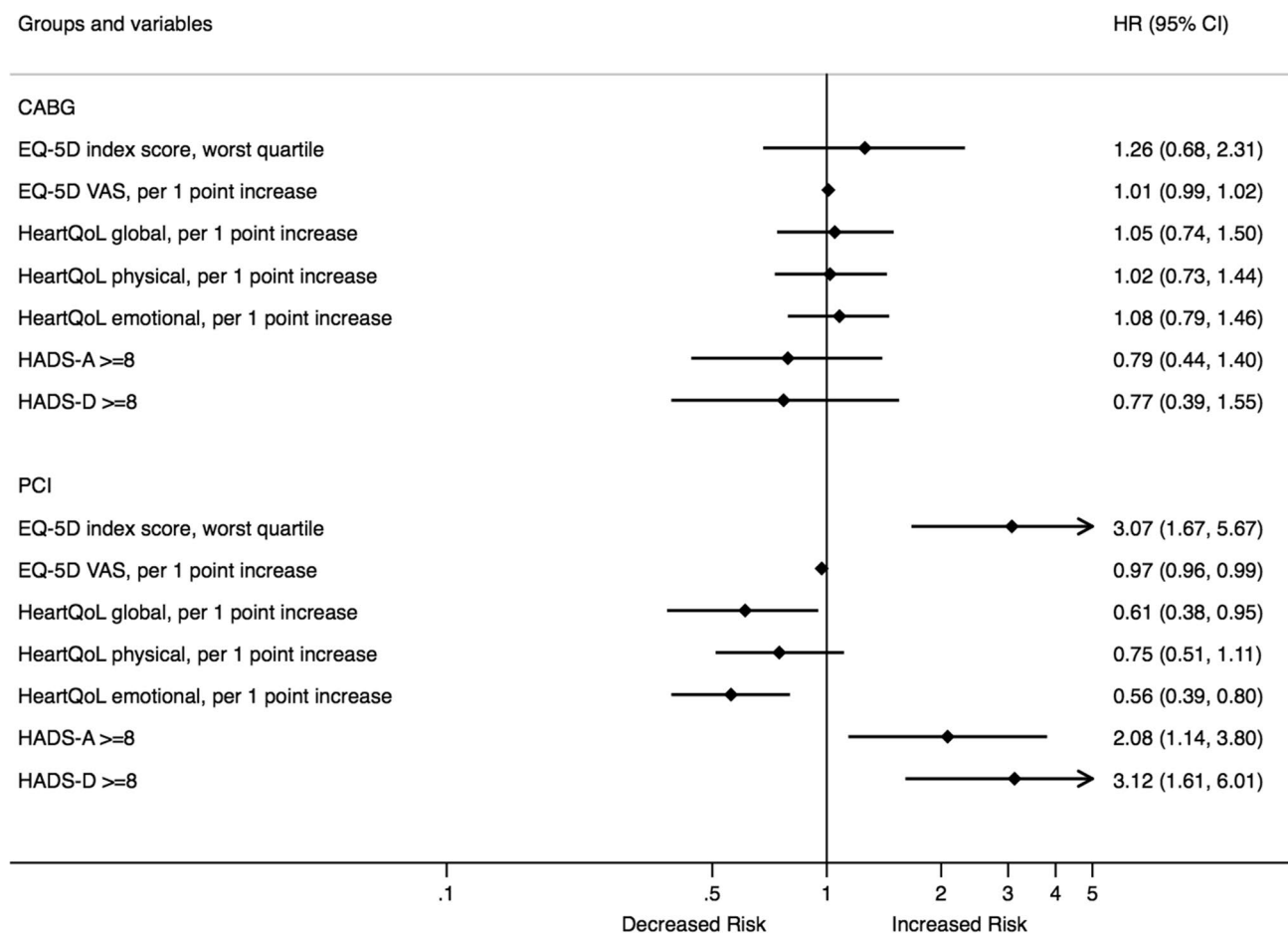


Fig. 3 Cox Proportional Hazard Models investigating the association between HRQoL, anxiety and depression and the risk of the composite endpoint of first acute, cardiac readmission, revascularisation or all-cause mortality (propensity-matched population). The analyses were adjusted for sex, age, COPD, prior PCI and current smoking

status. *EQ-5D* The European Quality of Life 5 Dimensions 5 Levels Questionnaire, *HADS* hospital anxiety and depression scale (*HADS-A* anxiety, *HADS-D*, depression). A higher score indicates a better health status on the EQ-5D VAS and HeartQoL, whereas a higher score on the HADS indicates worse status

matching was performed to ensure that almost all known variables were aligned between the groups, resulting in a more comparable result. Similarly, a strength of the study is the use of register-based data, as no patients were lost to follow-up, and the Danish registers are known to have a high validity [24–26].

Even though a thorough propensity matching was performed, only known variables were included in the matching, and therefore, unavailable confounders could potentially impact the results, including complexity and severity of coronary artery disease, LV function, frailty, functional class and pre-existing mental disorders. Our propensity matching represented nearly 10% of the total population and as being a responder was one of the matching criteria, the results were based on a selected population of patients. As patients needed to be alive at discharge to receive the questionnaire, mortality rates were calculated from discharge and thus, were lower than in comparable studies. Similarly,

confounding by indication may be a genuine problem with our study, although a propensity match was performed. This should be taken into account when interpreting the results.

Although the DenHeart study aimed to include all patients discharged from a Danish Heart Centre during the study period, the non-response rate in the overall study was 49% [48]. This might cause a risk of non-response bias, a common concern in patient-reported outcomes research. When evaluating the differences between responders and non-responders, non-responders were older, had a higher comorbidity burden, and among the PCI group, non-responders were more often women. As these characteristics are known to be associated with poorer HRQoL [48, 49], we expect that non-responders would report worse outcomes. Thus, this is a limitation of the study, and the results might be underestimated. Furthermore, due to a low inclusion of patients (responders) in the propensity-matched population, statistical power might be a problem in the regression analyses due

to few events. Still, as the results are seemingly comparable to others, this might not cause a concern. A further limitation associated with this study is the lack of control for the increase in the familywise error rate in the reported analyses.

Finally, the survey was only handed out at one time point (at discharge), meaning that information on patient-reported outcomes before the revascularisation procedures or changes on the long term were not included, thus, it was not possible to adjust for baseline differences or investigate changes over time.

To conclude, patients receiving PCI report better HRQoL at discharge compared with a propensity-matched population of patients undergoing CABG. Readmission and mortality rates were similar among the two groups, whereas revascularisation rates were higher among patients receiving PCI. HRQoL, anxiety and depression were associated with the risk of the adverse events among patients receiving PCI, but not patients among undergoing CABG.

Based on the findings, patients who report reduced HRQoL, anxiety or depression following PCI might be offered a more extensive follow-up post-discharge to reduce adverse outcomes and thereby potentially increase quality of life. As similar studies investigating and comparing HRQoL, anxiety and depression, and this risk of adverse events following CABG vs PCI are sparse, replications of similar studies are encouraged.

Acknowledgements A special thanks to the patients who took their time to participate in the survey, and to the cardiac nurses involved in the data collection.

Funding None.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

References



1. Sanchis-Gomar, F., Perez-Quilis, C., Leischik, R., et al. (2016). Epidemiology of coronary heart disease and acute coronary syndrome. *Annals of Translational Medicine*, 4(13), 256. <https://doi.org/10.21037/atm.2016.06.33>. (publishedOnlineFirst:2016/08/09).
2. Sousa-Uva, M., Neumann, F. J., Ahlsson, A., et al. (2019). 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Journal of Cardio-Thoracic Surgery*, 55(1), 4–90. <https://doi.org/10.1093/ejcts/ezy289>. (publishedOnlineFirst:2018/08/31).
3. Head, S. J., Milojevic, M., Taggart, D. P., et al. (2017). Current practice of state-of-the-art surgical coronary revascularization. *Circulation*, 136(14), 1331–1345. <https://doi.org/10.1161/CIRCULATIONAHA.116.022572>. (publishedOnlineFirst:2017/10/04).
4. Byrne, R. A., Stone, G. W., Ormiston, J., et al. (2017). Coronary balloon angioplasty, stents, and scaffolds. *Lancet*, 390(10096), 781–792. [https://doi.org/10.1016/S0140-6736\(17\)31927-X](https://doi.org/10.1016/S0140-6736(17)31927-X). (publishedOnlineFirst:2017/08/24).
5. Mulukutla, S. R., Gleason, T. G., Sharbaugh, M., et al. (2019). Coronary bypass versus percutaneous revascularization in multivessel coronary artery disease. *Annals of Thoracic Surgery*, 108(2), 474–480. <https://doi.org/10.1016/j.athoracsur.2019.02.064>. (publishedOnlineFirst:2019/05/06).
6. Makikallio, T., Holm, N. R., Lindsay, M., et al. (2016). Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. *Lancet*, 388(10061), 2743–2752. [https://doi.org/10.1016/S0140-6736\(16\)32052-9](https://doi.org/10.1016/S0140-6736(16)32052-9). (publishedOnlineFirst:2016/11/05).
7. Mohr, F. W., Morice, M. C., Kappetein, A. P., et al. (2013). Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet*, 381(9867), 629–638. [https://doi.org/10.1016/S0140-6736\(13\)60141-5](https://doi.org/10.1016/S0140-6736(13)60141-5). (publishedOnlineFirst:2013/02/27).
8. Stone, G. W., Kappetein, A. P., Sabik, J. F., et al. (2019). Five-year outcomes after PCI or CABG for left main coronary disease. *The New England Journal of Medicine*, 381(19), 1820–1830. <https://doi.org/10.1056/NEJMoa1909406>. (publishedOnlineFirst:2019/09/29).
9. Baron, S. J., Chinnakondepalli, K., Magnuson, E. A., et al. (2017). Quality-of-life after everolimus-eluting stents or bypass surgery for left-main disease: results from the EXCEL trial. *Journal of the American College of Cardiology*, 70(25), 3113–3122. <https://doi.org/10.1016/j.jacc.2017.10.036>. (publishedOnlineFirst:2017/11/04).
10. McGrath, B. M., Norris, C. M., Hardwicke-Brown, E., et al. (2017). Quality of life following coronary artery bypass graft surgery vs. percutaneous coronary intervention in diabetics with multivessel disease: a five-year registry study. *European Heart Journal-Quality of Care and Clinical Outcomes*, 3(3), 216–223. <https://doi.org/10.1093/ehjqcco/qcw055>. (published Online First: 2017/08/26).
11. Kulik, A. (2017). Quality of life after coronary artery bypass graft surgery versus percutaneous coronary intervention: what do the trials tell us? *Current Opinion in Cardiology*, 32(6), 707–714. <https://doi.org/10.1097/HCO.0000000000000458>. (publishedOnlineFirst:2017/08/24).
12. Abdallah, M. S., Wang, K., Magnuson, E. A., et al. (2017). Quality of life after surgery or DES in patients with 3-vessel or left main disease. *Journal of the American College of Cardiology*, 69(16), 2039–2050. <https://doi.org/10.1016/j.jacc.2017.02.031>. (publishedOnlineFirst:2017/04/22).
13. Abdallah, M. S., Wang, K., Magnuson, E. A., et al. (2013). Quality of life after PCI vs CABG among patients with diabetes and multivessel coronary artery disease: a randomized clinical trial. *JAMA*, 310(15), 1581–1590. <https://doi.org/10.1001/jama.2013.279208>. (publishedOnlineFirst:2013/10/17).
14. Takagi, H., Ando, T., Umemoto, T., et al. (2017). Perioperative depression or anxiety and postoperative mortality in cardiac surgery: a systematic review and meta-analysis. *Heart and Vessels*, 32(12), 1458–1468. <https://doi.org/10.1007/s00380-017-1022-3>. (publishedOnlineFirst:2017/07/14).
15. Geulayov, G., Novikov, I., Dankner, D., et al. (2018). Symptoms of depression and anxiety and 11-year all-cause mortality in men and women undergoing coronary artery bypass graft (CABG) surgery. *Journal of Psychosomatic Research*, 105, 106–114. <https://doi.org/10.1016/j.jpsychores.2017.11.017>. (publishedOnlineFirst:2018/01/16).
16. Stenman, M., Holzmann, M. J., & Sartipy, U. (2016). Association between preoperative depression and long-term survival following coronary artery bypass surgery—a systematic

- review and meta-analysis. *International Journal of Cardiology*, 222, 462–466. <https://doi.org/10.1016/j.ijcard.2016.07.216>. (publishedOnlineFirst:2016/08/10).
17. Yu, H. Y., Park, Y. S., & Son, Y. J. (2017). Combined effect of left ventricular ejection fraction and post-cardiac depressive symptoms on major adverse cardiac events after successful primary percutaneous coronary intervention: a 12-month follow-up. *European Journal of Cardiovascular Nursing*, 16(1), 37–45. <https://doi.org/10.1177/1474515116634530>. (publishedOnlineFirst:2016/02/19).
 18. Iles-Smith, H., McGowan, L., Campbell, M., et al. (2015). A prospective cohort study investigating readmission, symptom attribution and psychological health within six months of primary percutaneous coronary intervention. *European Journal of Cardiovascular Nursing*, 14(6), 506–515. <https://doi.org/10.1177/1474515114543227>. (publishedOnlineFirst:2014/07/16).
 19. Meyer, T., Hussein, S., Lange, H. W., et al. (2015). Anxiety is associated with a reduction in both mortality and major adverse cardiovascular events five years after coronary stenting. *European Journal of Preventive Cardiology*, 22(1), 75–82. <https://doi.org/10.1177/2047487313505244>. (publishedOnlineFirst:2013/09/21).
 20. van Dijk, M. R., Utens, E. M., Dulfer, K., et al. (2016). Depression and anxiety symptoms as predictors of mortality in PCI patients at 10 years of follow-up. *European Journal of Preventive Cardiology*, 23(5), 552–558. <https://doi.org/10.1177/2047487315571889>. (publishedOnlineFirst:2015/02/11).
 21. de Jager, T. A. J., Dulfer, K., Radhoe, S., et al. (2018). Predictive value of depression and anxiety for long-term mortality: differences in outcome between acute coronary syndrome and stable angina pectoris. *International Journal of Cardiology*, 250, 43–48. <https://doi.org/10.1016/j.ijcard.2017.10.005>. (publishedOnlineFirst:2017/10/11).
 22. Berg, S. K., Svanholm, J., Lauberg, A., et al. (2014). Patient-reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with a register-based follow-up: the DenHeart study protocol. *British Medical Journal Open*, 4(5), e004709. <https://doi.org/10.1136/bmjopen-2013-004709>. (publishedOnlineFirst:2014/05/06).
 23. NOMESCO, N. (2011). NOMESCO Classification of Surgical Procedures (NCSP), version 1.16. Copenhagen. Retrieved from <http://urn.kb.se/resolve?urn=urn:nbn:se:norden:org:diva-4605>.
 24. Pedersen, C. B. (2011). The danish civil registration system. *Scandinavian Journal of Public Health*, 39(7 Suppl), 22–25. <https://doi.org/10.1177/1403494810387965>. (publishedOnlineFirst:2011/08/04).
 25. Lynge, E., Sandegaard, J. L., & Rebolj, M. (2011). The danish national patient register. *Scandinavian Journal of Public Health*, 39(7 Suppl), 30–33. <https://doi.org/10.1177/1403494811401482>. (publishedOnlineFirst:2011/08/04).
 26. Jensen, V. M., & Rasmussen, A. W. (2011). Danish education registers. *Scandinavian Journal of Public Health*, 39(7 Suppl), 91–94. <https://doi.org/10.1177/1403494810394715>. (publishedOnlineFirst:2011/08/04).
 27. Tu, J. V., Austin, P. C., Walld, R., et al. (2001). Development and validation of the Ontario acute myocardial infarction mortality prediction rules. *Journal of the American College of Cardiology*, 37(4), 992–997. [https://doi.org/10.1016/s0735-1097\(01\)01109-3](https://doi.org/10.1016/s0735-1097(01)01109-3). (publishedOnlineFirst:2001/03/27).
 28. Rabin, R., & de Charro, F. (2001). EQ-5D: a measure of health status from the EuroQol Group. *Annals of Medicine*, 33(5), 337–343. <https://doi.org/10.3109/07853890109002087>. (publishedOnlineFirst:2001/08/09).
 29. Oldridge, N., Saner, H., McGee, H. M., et al. (2005). The Euro Cardio-QoL Project. An international study to develop a core heart disease health-related quality of life questionnaire, the HeartQoL. *European Journal of Cardiovascular Prevention & Rehabilitation*, 12(2), 87–94. <https://doi.org/10.1097/01.hjr.0000159408.05180.0e>. (published Online First: 2005/03/24).
 30. Oldridge, N., Hofer, S., McGee, H., et al. (2014). The HeartQoL: Part I. Development of a new core health-related quality of life questionnaire for patients with ischemic heart disease. *European Journal of Preventive Cardiology*, 21(1), 90–97. <https://doi.org/10.1177/2047487312450544>. (published Online First: 2012/07/24).
 31. Oldridge, N., Hofer, S., McGee, H., et al. (2014). The HeartQoL: part II. Validation of a new core health-related quality of life questionnaire for patients with ischemic heart disease. *European Journal of Preventive Cardiology*, 21(1), 98–106. <https://doi.org/10.1177/2047487312450545>. (published Online First: 2012/07/24).
 32. Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67(6), 361–370. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>. (publishedOnlineFirst:1983/06/01).
 33. De Smedt, D., Clays, E., Doyle, F., et al. (2013). Validity and reliability of three commonly used quality of life measures in a large European population of coronary heart disease patients. *International Journal of Cardiology*, 167(5), 2294–2299. <https://doi.org/10.1016/j.ijcard.2012.06.025>. (publishedOnlineFirst:2012/07/04).
 34. De Smedt, D., Clays, E., Hofer, S., et al. (2016). Validity and reliability of the HeartQoL questionnaire in a large sample of stable coronary patients: the EUROASPIRE IV study of the European society of cardiology. *European Journal of Preventive Cardiology*, 23(7), 714–721. <https://doi.org/10.1177/2047487315604837>. (publishedOnlineFirst:2015/09/12).
 35. WMA. (1964). Declaration of Helsinki. In H. 18th WMA General Assembly, Finland (Ed.), (Vol. 18th).
 36. Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. *Biometrika*, 70(1), 41–55.
 37. Thoemmes, F. J., & Kim, E. S. (2011). A systematic review of propensity score methods in the social sciences. *Multivariate Behavioral Research*, 46(1), 90–118. <https://doi.org/10.1080/00273171.2011.540475>. (publishedOnlineFirst:2011/02/07).
 38. Prentice, R. L., Kalbfleisch, J. D., Peterson, A. V., Jr., et al. (1978). The analysis of failure times in the presence of competing risks. *Biometrics*, 34(4), 541–554. (published Online First: 1978/12/01).
 39. Fine, J. P., & Gray, R. J. (1999). A proportional hazards model for the subdistribution of a competing risk. *Journal of the American statistical association*, 94(446), 496–509.
 40. Vaccarino, V., Badimon, L., Bremner, J. D., et al. (2019). Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. *European Heart Journal*. <https://doi.org/10.1093/eurheartj/ehy913>.
 41. Xiao, Y., Li, W., Zhou, J., et al. (2019). Impact of depression and/or anxiety on patients with percutaneous coronary interventions after acute coronary syndrome: a protocol for a real-world prospective cohort study. *British Medical Journal Open*, 9(9), e027964. <https://doi.org/10.1136/bmjopen-2018-027964>. (publishedOnlineFirst:2019/09/08).
 42. Berg, S. K., Rasmussen, T. B., Herning, M., et al. (2019). Cognitive behavioural therapy significantly reduces anxiety in patients with implanted cardioverter defibrillator compared with usual care: Findings from the Screen-ICD randomised controlled trial. *European Journal of Preventive Cardiology*. <https://doi.org/10.1177/2047487319874147>. (published Online First: 2019/10/03).

43. Borregaard, B., Pedersen, S. S., Berg, S. K., et al. (2019). What to expect after open heart valve surgery? Changes in health-related quality of life. *Quality of Life Research*. <https://doi.org/10.1007/s11136-019-02400-9>. (published Online First: 2019/12/26).
44. Borregaard, B., Sorensen, J., Ekholm, O., et al. (2018). Sociodemographic, clinical and patient-reported outcomes and readmission after heart valve surgery. *The Journal of Heart Valve Disease*, 27(1), 78–86. (published Online First: 2018/12/19).
45. Berg, S. K., Thorup, C. B., Borregaard, B., et al. (2019). Patient-reported outcomes are independent predictors of one-year mortality and cardiac events across cardiac diagnoses: findings from the national DenHeart survey. *European Journal of Preventive Cardiology*, 26(6), 624–637. <https://doi.org/10.1177/2047487318769766>. (published Online First: 2018/04/12).
46. Vamosi, M., Lauberg, A., Borregaard, B., et al. (2019). Patient-reported outcomes predict high readmission rates among patients with cardiac diagnoses. Findings from the DenHeart study. *International Journal of Cardiology*. <https://doi.org/10.1016/j.ijcar.2019.09.046>. (published Online First: 2019/11/22).
47. Zhang, W. Y., Nan, N., Song, X. T., et al. (2019). Impact of depression on clinical outcomes following percutaneous coronary intervention: a systematic review and meta-analysis. *British Medical Journal Open*, 9(8), e026445. <https://doi.org/10.1136/bmjopen-2018-026445>. (published Online First: 2019/08/23).
48. Berg, S. K., Rasmussen, T. B., Thrysoee, L., et al. (2017). DenHeart: differences in physical and mental health across cardiac diagnoses at hospital discharge. *Journal of Psychosomatic Research*, 94, 1–9. <https://doi.org/10.1016/j.jpsychores.2017.01.003>. (published Online First: 2017/02/12).
49. Munyombwe, T., Hall, M., Dondo, T. B., et al. (2020). Quality of life trajectories in survivors of acute myocardial infarction: a national longitudinal study. *Heart*, 106(1), 33–39. <https://doi.org/10.1136/heartjnl-2019-315510>. (published Online First: 2019/11/09).

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Affiliations

Stine Nørris Nielsen^{1,2}  · Trine Bernholdt Rasmussen³ · Jens Flensted Lassen^{1,2} · Selina Kikkenborg Berg^{4,5} · Lars Thrysoee^{1,2} · Jacob Eifer Møller^{1,2} · Lisette Okkels Jensen^{1,2} · Anne Langhoff Thuesen⁶ · Anne Vinggaard Christensen⁴ · Ola Ekholm⁷ · Rikke Mols⁸ · Charlotte Brun Thorup⁹ · Britt Borregaard^{1,2,6} 

¹ Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark

² University of Southern Denmark, Odense, Denmark

³ Department of Cardiology, Herlev and Gentofte University Hospital, Hellerup, Denmark

⁴ Department of Cardiac, Vascular, Pulmonary and Infectious Diseases, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

⁵ University of Copenhagen, Copenhagen, Denmark

⁶ Department of Cardiac, Thoracic and Vascular Surgery, Odense University Hospital, Odense, Denmark

⁷ National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark

⁸ Department of Cardiology, Aarhus University Hospital, Skejby Sygehus, Aarhus, Denmark

⁹ Department of Cardiology, Cardiothoracic Surgery and Clinical Nursing Research Unit, Aalborg University Hospital, Aalborg, Denmark