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Association between frailty and self-reported health following heart valve surgery

Britt Borregaard [a,b,c,1,*], Jordi S. Dahl [a,c,1], Sandra B. Lauck [d,e,1], Jesper Ryg [c,f,1], Selina K. Berg [g,h,1], Ola Ekholm [c,1], Jeroen M. Hendriks [i,j,k,1], Lars P.S. Riber [b,c,1], Tone M. Norekvål [l,m,n,1], Jacob E. Møller [a,c,h,1]

[a] Department of Cardiology, Odense University Hospital, Denmark
[b] Department of Cardiothoracic and Vascular Surgery, Odense University Hospital, Denmark
[c] University of Southern Denmark, Denmark
[d] Centre for Heart Valve Innovation, St. Paul's Hospital, Canada
[e] University of British Columbia, Canada
[f] Department of Geriatric Medicine, Odense University Hospital, Denmark
[g] Department of Clinical Medicine, University of Copenhagen, Denmark
[h] The Heart Centre, Rigshospitalet, Copenhagen University Hospital, Denmark
[i] Centre for Heart Rhythm Disorders, South Australian Health and Medical Research Institute, Royal Adelaide Hospital, Australia
[j] College of Nursing and Health Sciences, Flinders University, Australia
[k] Department of Health, Medicine and Caring Sciences, Linköping University, Sweden
[l] Department of Heart Disease, Haukeland University Hospital, Norway
[m] Department of Clinical Science, University of Bergen, Norway
[n] Department of Health and Caring Sciences, Western Norway University of Applied Sciences, Norway

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ABSTRACT

Background: Knowledge about the association between frailty and self-reported health among patients undergoing heart valve surgery remains sparse. Thus, the objectives were to I) describe changes in self-reported health at different time points according to frailty status, and to II) investigate the association between frailty status at discharge and poor self-reported health four weeks after discharge among patients undergoing heart valve surgery.

Methods: In a prospective cohort study, consecutive patients undergoing heart valve surgery, including transapical/transaortic valve procedures were included. Frailty was measured using the Fried score, and self-reported health using the Kansas City Cardiomyopathy Questionnaire (KCCQ) and the EuroQoL-5 Dimensions 5-Levels Health Status Questionnaire (EQ-5D-5L).

To investigate the association between frailty and self-reported health, multivariable logistic regression models were used. Analyses were adjusted for sex, age, surgical risk evaluation (EuroScore) and procedure and presented as odds ratios (OR) with 95% confidence intervals (CI).

Results: Frailty was assessed at discharge in 288 patients (median age 71, 69% men); 51 patients (18%) were frail. In the multivariable analyses, frailty at discharge remained significantly associated with poor self-reported health at four weeks, OR (95% CI): EQ-5D-5L Index 3.38 (1.51–7.52), VAS 2.41 (1.13–5.14), and KCCQ 2.84 (1.35–5.97).

Conclusion: Frailty is present at discharge in 18% of patients undergoing heart valve surgery, and being frail is associated with poor self-reported health at four weeks of follow-up. This supports a clinical need to address the unique risk of frail patients among heart valve teams broadly, and not only to measure frailty as a marker of operative risk.

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1. Introduction

Frailty reflects a multidimensional state of decreased physiological reserves, a vulnerability towards pathological stressors, and a loss of adaptive capacity [1–3]. Elements of frailty commonly include lowered activity level, loss of muscle strength, uninten-

* Corresponding author at: Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark.
E-mail address: britt.borregaard@rsyd.dk (B. Borregaard).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

tional weight loss, and self-reported exhaustion [4,2]. These elements represent an overall marker of the functional and physical condition of the patient [4,5], and combined; frailty status describes a patient's physiological reserves and resistance to stressors [2].

Among patients with severe heart valve disease, the 2017-European guidelines on the management of valvular heart disease recommend assessment of frailty status before surgery as a strategy for stratifying patients at risk of poor outcomes [6]. Similarly, there is a growing body of evidence demonstrating that preoperative frailty is associated with mortality, morbidity, and functional decline after aortic valve replacement, mainly investigated in patients undergoing transcatheter aortic valve replacement (TAVR) [7–9].

Regardless of the choice of procedure (e.g., TAVR procedure or open heart valve surgery), frail patients are known to have worse self-reported health compared with non-frail patients [10,11]. Nevertheless, evidence demonstrating whether frail patients perceive similar improvements in self-reported health status post-surgery as non-frail patients remain sparse and current studies fails to include patients who require surgical treatment [10,11]. Although transcatheter approaches are increasingly used to treat various valvular heart diseases, surgical approaches remain the standard of care for a large group of patients; accordingly, this warrants further investigation of the prognosis and recovery trajectory of frail patients after discharge in the setting of surgical treatment of valvular heart disease.

Thus, in a population of patients undergoing heart valve surgery the objectives were to I) describe changes in self-reported health at different time points according to frailty status, and to II) investigate the association between frailty status at discharge and poor self-reported health four weeks after discharge.

2. Methods

2.1. Study design

A prospective cohort study investigating the association between frailty status and self-reported health among patients undergoing heart valve surgery.

The study is a pre-defined sub-study of the findings of the *Individualised Follow-up after Valve Surgery* (INVOLVE) study [12]. The INVOLVE study was a prospective cohort study comparing a composite endpoint of the first event of unplanned cardiac hospital readmissions or all-cause mortality in patients undergoing early, individualised, and intensified follow-up after heart valve surgery with a propensity-matched historical control group [12]. In the current sub-study, the association between frailty status and self-reported health following heart valve surgery among the intervention group of INVOLVE was investigated. Furthermore, additional data on frailty assessment at three different time points was performed in a consecutively selected sub-population (n = 120).

2.2. Participants and setting

Consecutive patients undergoing heart valve surgery (conventional trans-sternal surgery (replacement or repair) or transapical or transaortic TAVR) were enrolled in the intervention from November 2016 – November 2017, at Odense University Hospital, Denmark. The sub-population was included from May 2017 to November 2017. Patients were included based on their surgical procedure codes [13]: Aortic (KFCA, KFMA, KFMC, KFMD), Mitral (KFKB, KFKC, KFKD, KDKW) and Tricuspid (KFGC, KFGE).

Patients with disabling perioperative stroke and patients undergoing surgery due to infective endocarditis were not eligible for inclusion (Fig. 1). Patients undergoing transfemoral TAVR were not included in the current study.

2.3. Data collection

2.3.1. Demographic and clinical data

Demographics and clinical characteristics were obtained from hospital records and the Western Denmark Heart Registry [14]. Living status, body mass index (BMI), alcohol consumption, smoking status and length of stay were obtained from the electronic medical records, while comorbidity, the type of surgery, and EuroScore II (surgical risk evaluation) were obtained from WDHR. The EuroScore II is a logistic surgical risk evaluation calculated before surgery including age, sex, renal impairment, extracardiac arteriopathy, poor mobility, chronic lung disease, active endocarditis, critical pre-operative state, angina status, recent myocardial infarction, pulmonary hypertension, urgency and weight of the procedure [15].

2.3.2. Frailty assessment

Frailty status was assessed at discharge with a modified version of the frailty phenotype by Fried [4] including; unintentional weight loss, feelings of exhaustion, weakness (grip strength), gait speed, and independence in Activities of Daily Living (ADL) measured with the Katz Index [16]. Cut-off scores, as defined by Fried, were used for gait speed and grip strength [4].

The overall frailty status of the patient was assessed based on the above domains. Patients with problems in ≥ 3 domains were considered as frail [4].

Further, in the sub-population of 120 consecutively included patients, frailty was assessed preoperatively, at discharge and four weeks after discharge.

2.3.3. Self-reported health

The following patient-reported outcome measurements were included: The EuroQoL-5 Dimensions 5-Levels Health Status Questionnaire (EQ-5D-5L), and the Kansas City Cardiomyopathy Questionnaire (KCCQ), 12-item [17,18]. The measurements were handed out on the day before surgery (baseline), at discharge and four weeks after discharge. Due to two weeks recall, KCCQ was only handed out at baseline and four weeks, whereas EQ-5D-5L was handed out at all time points.

The EQ-5D-5L assesses generic health with an Index Score and a Visual Analogue Scale, VAS, and has proven high validity and performance among patients undergoing heart valve surgery [17,19]. Higher scores indicate better health. Minimal clinically important differences (MCID) has been reported to be 0.10/0.125 (index score) and 8.61 (VAS) [20,19].

The KCCQ is a disease-specific questionnaire assessing four domains, and combined into an overall summary score (0–100). Higher scores indicate better health and low symptom burden [18]. The original KCCQ is validated among patients with aortic stenosis [21]. A MCID of 5 points for the KCCQ has previously been detected [18].

Supplementary Table S1 illustrates the measurement of frailty status and self-reported health at different time points.

2.4. Outcomes

Poor self-reported health measured with the EQ-5D-5L was defined as the composite of: 1) a score within the worst quartile
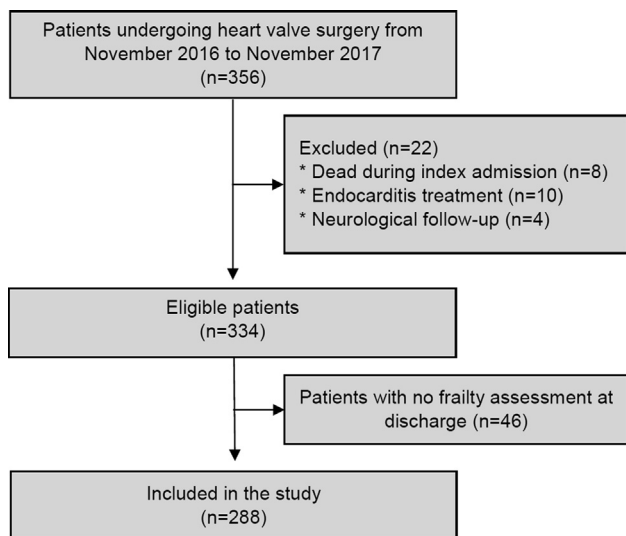
Fig. 1. Study Flowchart.

of scores, and/or, 2) a decrease in scores from baseline to four weeks after discharge of more than the MCID.

Poor self-reported health with the KCCQ was defined as a composite of: 1) a score < 45 measured with the overall summary score (KCCQ-OS) score, and/or 2) a decrease of $\geq$ 10 points in the KCCQ-OS score from baseline to four weeks after discharge [22].

2.5. Statistical analyses

Baseline characteristics are presented as numbers and proportions, and median with 25th to 75th percentiles (interquartile range, IQR), as appropriate. Due to non-normally of data, the Mann-Whitney U test was used to compare continuous data, whereas categorical variables were compared using the χ^2 test.

Differences in proportions of patients having problems within the different elements of the frailty test were investigated among non-frail and frail patients using the χ^2 test and plotted as a radar chart. The proportion of patients being frail before surgery, at discharge and four weeks after discharge were investigated in the sub-population.

Due to the skewed distribution of scores of self-reported health, these were presented as median and IQR, and non-parametric tests were applied to analyse these data. Differences in median scores of the EQ-5D-5L preoperatively, at discharge, and four weeks after discharge among non-frail and frail patients were tested with the Wilcoxon signed-rank test (paired), similar as the differences in scores of the KCCQ preoperatively and four weeks after discharge. Changes in mean scores of both EQ-5D-5L and KCCQ at different time point were analysed with the paired-samples t-test.

Univariable and multivariable logistic regression models were used to assess the association between being frail (vs non-frail) and poor self-reported health. Each instrument was adjusted for sex, age, EuroScore II, and TAVR procedure (as this was expected to influence frailty status) in the multivariable regression models. Results are presented as odds ratios (OR) with 95% confidence intervals (CI).

The interaction between the patients undergoing surgical and transapical procedures on poor self-reported health was assessed separately in post-hoc analyses.

A two-sided value of p < 0.05 was considered as statistically significant. The statistical analyses were performed using STATA 14.2 (StataCorp, College Station, TX, USA) and SPSS 24 (IBM Corp. Armonk, NY).

2.6. Ethics approval

The investigation conformed with the principles outlined in the Declaration of Helsinki. The study was approved by the Danish Data Protection Agency (18/19152). All patients received oral and written information and provided written consent.

3. Results

3.1. Study population

Among 334 patients enrolled in the prospective study, 288 patients (86%) had a frailty assessment at discharge (median age 71, 69% men, 64% were diagnosed with aortic stenosis) and were included in the current study (Fig. 1). Of those, 51 (18%) were frail, and among patients above the age of 70, n = 41 (24%) were frail. Compared to non-frail patients, frail patients were more likely to be women (53% vs 26%, p < 0.001), were older (median 78 years vs 70 years, p < 0.001), and living alone (43% vs 22%, p < 0.001) (Table 1). In addition, several clinical and procedural differences were found among non-frail and frail patients, including a higher proportion of frail patients having a EuroScore II $\geq$ 2 (71% vs 44%, p < 0.001) and an estimated glomerular filtration rate $\leq$ 60 (49% vs 22%, p < 0.001) (Table 1). The proportion of patients being frail was highest at discharge and was significantly reduced at follow-up one month after discharge (Supplementary Fig. S1). Also, among the frail patients, the proportion of patients experiencing problems within each area included; shrinking (33%), exhaustion (86%), weakness (77%), slowness (78%), and ADL (73%) (Fig. 2, Supplementary Table S2).

Table 1
Demographic and clinical characteristics.

	Non-frail (n = 237)	Frail (n = 51)	p*
Characteristics			
Sex, female, n (%)	62 (26)	27 (53)	<0.001
Age, median (IQR)	70 (63;75)	78 (72;83)	<0.001
Living alone, n (%)	52 (22)	22 (43)	0.002
Patient characteristics			
Reduced pulmonary function[a], n (%)	85 (36)	24 (47)	0.135
EuroScore II $\geq$ 4, n (%)	50 (21)	23 (45)	<0.001
Estimated glomerular filtration rate ml/min.[b] $\leq$ 60, n (%)	53 (22)	25 (49)	<0.001
Prior cardiac surgery, n (%)	24 (11)	11 (22)	0.030
Permanent pacemaker, n (%)	11 (5)	<5	0.720
Ejection fraction $\leq$ 50%, n (%)	73 (31)	19 (37)	0.370
NYHA class $\geq$ 2, n (%)	223 (94)	50 (98)	0.484
Body Mass Index, median (IQR)	26 (23;29)	26 (22;28)	0.064
Type of valve procedure, n (%)			
Aortic valve, surgical replacement or repair	186 (79)	31 (61)	0.008
TAVR[f] (transaortic/ transapical)	11 (5)	11 (22)	<0.001
Mitral valve, surgical replacement or repair	39 (17)	9 (18)	0.836
Concomitant CABG + aortic valve surgery	39 (17)	9 (18)	0.836
Concomitant CABG + mitral valve surgery	6 (3)	<5	0.584
Post-operatively			
Re-operation, n (%)	14 (6)	9 (18)	0.010
Length of stay, intensive care unit, median (IQR)	1 (1;1)	1 (1;2)	<0.001
Length of stay, median (IQR)	9 (7;11)	12 (8;19)	<0.001

P < 0.05 is considered as statistically significant.
[a] Forced expiratory volume,% $\leq$80% of predicted value and/or a history of chronic obstructive pulmonary disease.
[b] Estimated by the Cockcroft-Gault Equation.

3.2. Differences and changes in self-reported health among frail and non-frail patients

Self-reported health measured with the EQ-5D-5L Index score, the EQ-5D-5L VAS score, and the KCCQ were significantly better among non-frail and frail patients before surgery, at discharge, and four weeks after discharge (Table 2).

Non-frail patients experienced a significant reduction in the EQ-5D-5L Index scores between the preoperative assessment and discharge (EQ-5D-5L Index Δ-0.05, 95% CI −0.07 − −0.03) and a significant increase between discharge and four weeks post-discharge on both the EQ-5D-5L Index score and VAS (EQ-5D-5L Index score Δ0.05, 95% CI 0.03–0.07, VAS Δ10, 95% CI 7–13). Although statistically significant, the changes only reached a clinically important difference for the EQ-5D-5L VAS. Scores of the EQ-5D-5L VAS and the KCCQ significantly increased from the preoperative assessment to four weeks after discharge (VAS Δ7, 95% CI 4–10 and KCCQ Δ9.94, 95% CI 6.86–13.01), reaching a clinically important difference for the KCCQ (Fig. 3, Supplementary Table S3). Contrary, among frail patients, a statistically significant improvement from discharge to four weeks after discharge was shown on the EQ-5D-5L Index and the EQ-5D-5L VAS (Index Δ0.08, 95% CI 0.02–0.13, VAS Δ11, 95% CI 5–18), but not on the KCCQ (Fig. 3, Supplementary Table S3). The scores of the EQ-5D-5D VAS reached a clinically important difference. Relative changes (%) in scores among frail and non-frail patients from baseline to discharge and four weeks after discharge did not significantly differ (Fig. 4).

3.3. Association between frailty and poor self-reported health four weeks after discharge

In the logistic regression models, being frail vs non-frail was significantly associated with poor self-reported health in the adjusted analyses (OR (95% CI)) on the EQ-5D-5L Index (3.38 (1.51–7.52)), the EQ-5D-5L VAS (2.41 (1.13–5.14)), and the KCCQ (2.84 (1.35–5.97)). The analyses were adjusted for sex, age, EuroScore and TAVR procedure. Crude and adjusted analyses are presented in Table 3.

The results of the post-hoc analyses revealed no statistically significant interactions between the surgical and the transapical patients on poor self-reported health (p-value of the interactions; EQ-5D 5L Index 0.364, VAS 0.873, KCCQ 0.236).

4. Discussion

In this prospective study, we investigated the association between frailty and poor self-reported health in a population of patients undergoing heart valve surgery. Nearly one out of five was frail at discharge. Main problem areas among the frail population were exhaustion, weakness, and slowness. In addition, frail patients reported significantly lower scores of health and frailty was independently associated with worse self-reported health on all measures.

Several studies have demonstrated the proportion of patients being frail when undergoing heart valve surgery, but tend to focus on preoperative frailty assessments [7,11,23]. Previously, Afilalo et al. have demonstrated how 25% of patients above 70 years undergoing surgical aortic valve replacement are frail measured with the Fried frailty score at different time points (during admission and in outpatient clinics) [24]. This is comparable with 24% of patients above 70 years being frail in our study. To our knowledge, though, the current study is the first study to investigate frailty status at discharge in a consecutive population of patients following heart valve surgery. Although only measured in a sub-population of 120 patients, we have demonstrated how the proportion of patients being frail at the time of discharge is higher than before surgery – and reduces again after four weeks. As this highlights how frailty is a dynamic state, it might be an essential measure of the post-procedural pathway and the knowledge of the surgical procedure on physical changes can guide clinicians on expected
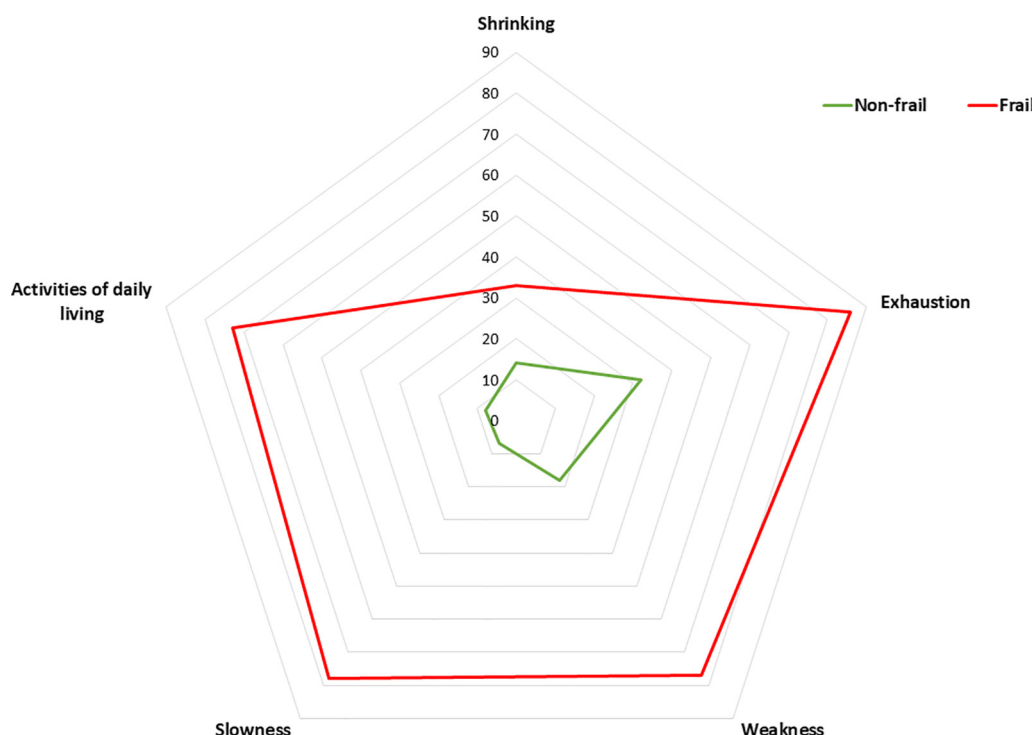

Fig. 2. The proportion of patients with problems within the specific domains of the Fried Frailty Scale. The figure plots the proportion of problems within the specific areas among non-frail and frail patients with the use of a radar plot.

Table 2
Differences in scores of self-reported health status among non-frail and frail patients.

Median (IQR)	Non-frail (n = 237)	Frail (n = 51)	p
Preoperative			
EQ-5D-5L			
Index score	0.79 (0.71–0.86)	0.70 (0.63–0.81)	<0.001
VAS score	70 (50–80)	61 (41–74)	0.002
KCCQ			
Summary score	64.6 (47.9–78.1)	58.9 (41.4–68.0)	0.018
Discharge			
EQ-5D-5L			
Index score	0.75 (0.67–0.81)	0.65 (0.57–0.73)	<0.001
VAS score	70 (50–80)	50 (40–61.25)	<0.001
Four weeks after discharge			
EQ-5D-5L			
Index score	0.80 (0.75–0.86)	0.73 (0.66–0.79)	<0.001
VAS score	80 (66–87)	70 (60–75)	<0.001
KCCQ			
Summary score	77.6 (62.5–87.5)	61.2 (49.5–75.0)	<0.001

outcomes. Thus, although not previously investigated, post-surgical measurements of frailty might be a useful marker of the clinical pathway.

Notably, while one-third of the frail patients were experiencing problems within the overall area "shrinking", this was also the area where fewest frail patients had problems. Due to the metabolic stress of the surgery, more patients were expected to experience problems within this area; however, problems with exhaustion, weakness, and slowness dominated the frail population. Previous studies have demonstrated how the most effective way to improve the status of frail patients is exercise and physical rehabilitation, as it improves balance (and prevent falls), increase gait speed and improve overall performance in ADL functions [25,26]. Currently, the PERFORM-TAVR trial is testing an intervention consisting of a home-based exercise programme in combination with nutritional supplements on physical performance [27]. Similarly, the FOCUS-recommendations suggest interventions to include physical activity, nutritional interventions or a combination, to prevent, delay or reverse frailty [28]. In general, though, there is a need for high-quality studies investigating interventions with the potential to affect frailty [28]. Consequently, to reverse and change outcomes among frail patients, interventions should be aimed at the specific problem areas.

While the risk of morbidity and mortality increases with age and frailty status, potential gains in health status are important measures to include in the overall assessment of a patient. We demonstrated the importance of such assessment by demonstrating an association between frailty at discharge and the risk of poor self-reported health four weeks after discharge. When measuring health status with a disease-specific measurement (KCCQ), frail patients do not show the same increase in scores as non-frail patients from before surgery to four weeks, why an effort in improving these outcomes should be performed. Contrary, on the EQ-5D-5L VAS scale, both non-frail and frail patients experienced an improvement of more than the clinical minimal importance difference measured from discharge to four weeks after. These findings correspond to previous studies, although improvements were demonstrated based on a longer follow-up period [10,23]. Surprisingly, the findings combined suggest that overall improvements in generic self-reported health remain similar, despite frail patients having lower scores. We expect that the surgical procedure influence patients being frail to a greater extent than non-frail patients, due to the vulnerability towards stressors, and frail patients might, therefore, experience more symptoms related to the disease and the surgery. This might explain the lack of improvement in disease-specific self-reported health. Accordingly,
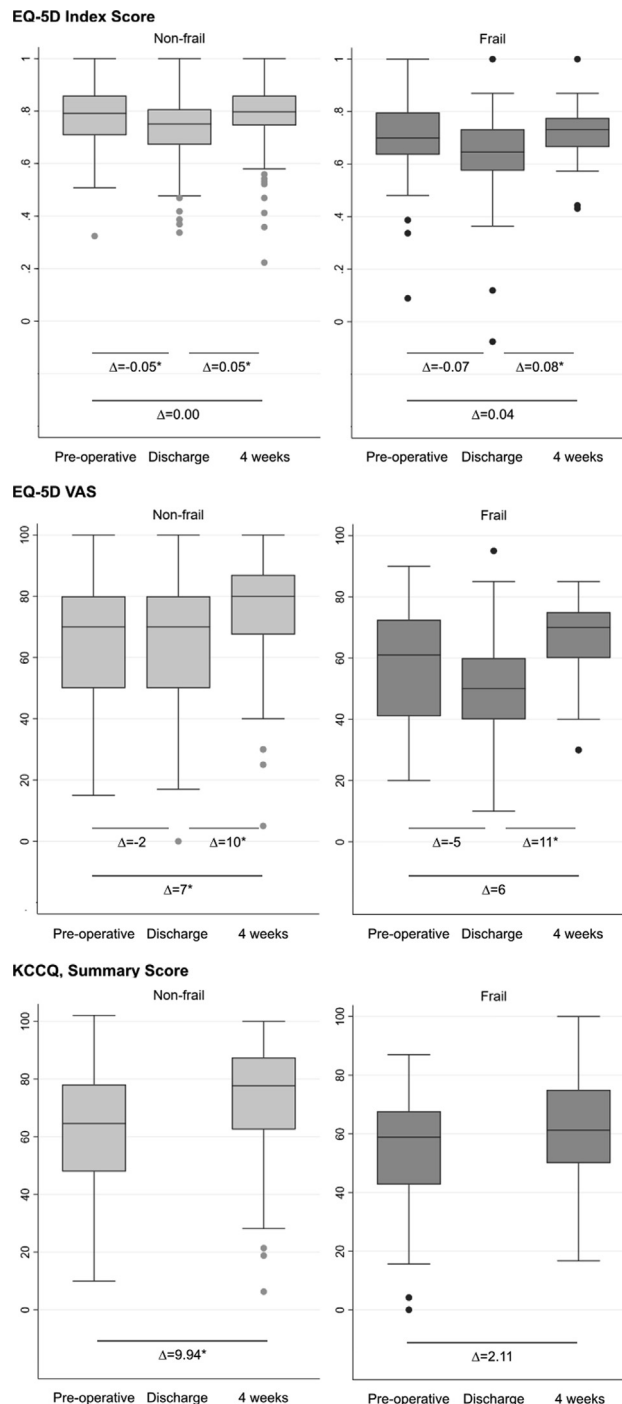
Fig. 3. Changes in scores of the EQ-5D-5L and the KCCQ among non-frail and frail patients. The figure illustrates changes in self-reported health among non-frail and frail patients, including mean change in scores on the different time points. * P < 0.05 is considered as statistically significant.

follow-up among frail patients should be targeted the disease-specific symptoms.

Finally, although a clear "gold standard" when measuring frailty is missing, and some studies have highlighted how the "eyeball test" might supplement objective measurement among patients with aortic stenosis [29,30], a more systematic approach is needed to support the recovery trajectories of the patients [31]. Besides risk stratification before surgery, the current study showed how a frailty assessment at discharge could stratify patients at higher risks of poor outcomes when going home. Also, we acknowledge
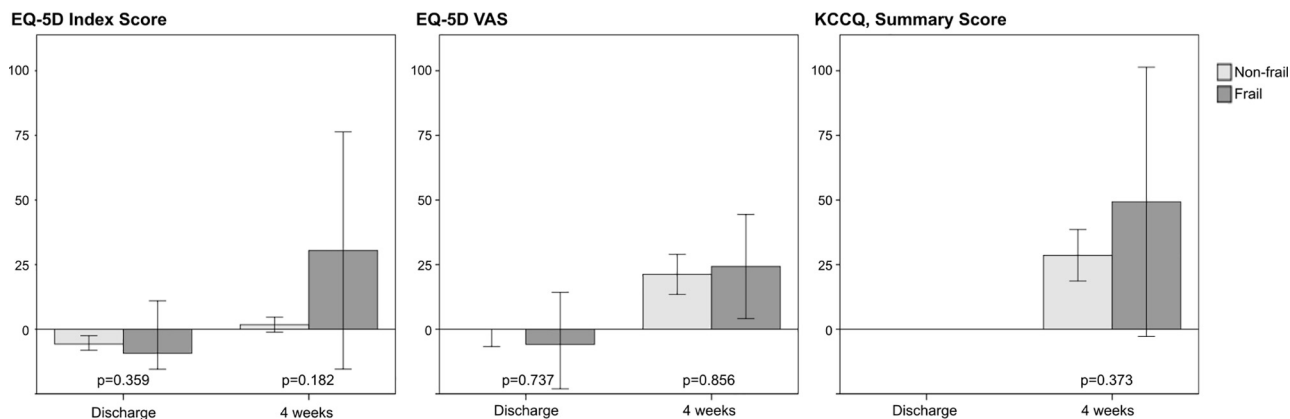
Fig. 4. Relative changes, percentage, in scores at different time point among non-frail and frail patients. The figure illustrates relative changes (%) in self-reported health status from baseline to discharge and four weeks after discharge among non-frail and frail patients. Self-reported health was only measured at two time points on the KCCQ and thus, not illustrated from baseline to discharge. * P < 0.05 is considered as statistically significant.

Table 3
The association between frailty at discharge and poor self-reported health status four weeks after discharge.

	Crude OR (CI)	Adjusted OR (CI)
EQ-5D-5L index, poor outcomes		
Frail vs non-frail	2.46 (1.20–5.05)	3.38 (1.51–7.52)
EQ-5D-5L VAS, poor outcomes		
Frail vs non-frail	2.14 (1.07–4.27)	2.41 (1.13–5.14)
KCCQ, poor outcomes		
Frail vs non-frail	2.14 (1.10–4.16)	2.84 (1.35–5.97)

Adjusted for sex, age, EuroScore and TAVR procedure.

how the assessment of frailty may include more than physical elements, as characteristics such as cognition and social support are known to influence outcomes [32]. Future studies are encouraged to include a broader frailty assessment when investigating outcomes among patients with valvular heart disease.

4.1. Strength and limitations

The main strength of the study is the use of prospective data on frailty status and self-reported health and the investigation of frailty status at discharge – also among a surgical population. Combined, this adds to the current knowledge of the clinical pathway following heart valve surgery. Similarly, a strength of the study is the inclusion of both generic and disease-specific measurements of self-reported health. As these instruments seem to detect different trajectories, the inclusion of both strengthens the findings.

In total, 46 patients (14%) did not receive a frailty assessment due to early discharge without the involvement of research personnel. These patients may potentially have influenced the results, but due to similar baseline characteristics (median age 71, 69% men, 73% underwent surgical aorta valve replacement, 8% TAVR-procedure), this is unlikely. Patients receiving an alternative access TAVR-procedure were included as they are expected to have a clinical pathway following the procedure similar to those of patients undergoing a surgical procedure. We recognise, though, how a higher proportion of these patients might be frail, but as interaction analyses revealed no significant interactions between the surgical and the transapical groups, we have kept this group in the study. Frailty assessment at all time points among the total population and not only a consecutive sub-population would have strengthened the results. Also, the present study had no power to determine whether frailty status at discharge is of prognostic importance.

In general, the response rates of the questionnaires were high (77–92%) [33], and missing data were assumed to be missing at random, why the regression analyses were performed as a complete case analysis. Moreover, although the sample size is small, leading to a conservative estimate of the results, the change in median scores on the EQ-5D-5L did not reach a clinically important difference. Thus, the overall results are not expected to be different in a larger population.

In conclusion, frailty at discharge occurs in approximately one out of five patients while being frail is associated with poor self-reported health. However, frailty assessment in patients after heart valve surgery is scarce. Future research is needed to study integration of a standardised measurement of frailty to improve outcomes after heart valve surgery.

4.2. Implications for practice

The study underlined the association between being frail at discharge and worse self-reported health after four weeks. This knowledge supports a clinical need to address the unique risk of frail surgical patients among heart valve teams broadly, and not only to measure frailty as a marker of operative risk. A complex care plan of frail patients should be incorporated in the discharge planning, and frail surgical valve patients potentially require closer follow-up and targeted interventions to improve overall outcomes, frailty status and self-reported health. Also, to prevent further deterioration in physical capacity, an exercise plan, early in-hospital rehabilitation, and referral for rehabilitation following discharge should gain increased focus [34,35]. Despite the prognostic and therapeutic relevance, frailty is not routinely assessed among patients undergoing open heart valve surgery and the current study highlight how ongoing efforts must focus on improving both the measurement and the treatment of this health state – to improve the overall health outcome of the valve patient.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contribution

BBO, JD, and JEM designed the study. BBO conducted the analyses in collaboration with JD, JR and JEM. BBO drew up the first draft of the manuscript, tables and figures. All authors contributed to the

interpretation of data, revisions to the manuscript and approved the final version to be published.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2020.100671.

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