Outcome of osteoarthritis and arthroplasty from patient perspective to molecular profiling.

Meessen, J.M.T.A.

Frailty questionnaire is no predictor for functional outcomes in hip or knee arthroplasty patients

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Abstract

Introduction: Up to 33% and 25% of end-stage hip and knee osteoarthritis (OA) patients are considered frail by the Groningen Frailty Indicator (GFI).[1] This study aims to assess whether frail patients have lower functional gains after arthroplasty and to assess GFI as a tool to discriminate between good or adverse change-score.

Materials and Methods: End-stage hip/knee OA patients scheduled for arthroplasty were recruited from the LOAS-study. Functional outcome was measured as change-score on the Hip/Knee Osteoarthritis Outcome Score (HOOS/KOOS), by subtracting pre-operative score from 1-year post-surgery score and then dichotomised based on a cut-off of 20 points. For each HOOS/KOOS-subscale 3 models were estimated: GFI univariate (model 1), GFI and baseline-score (model 2) and baseline-score univariate (model 3). A ROC-analysis was performed to assess the discriminative ability of each model.

Results: 805 end-stage hip (31.4% frail) and 640 end-stage knee OA patients (25.4% frail) were included. Frail patients were older, had a higher BMI, more comorbidities and lived more often alone. Persons considered frail by GFI had significant lower baseline-score; however, except for “function in sports & recreation” and “quality of life” change-scores were similar in frail and non-frail persons. The discriminatory value of GFI was negligible for all HOOS/KOOS-subscales. Baseline score, however, was adequate to discriminate between TKA patients with more or less than twice the minimal clinical important difference (MCID) on KOOS-symptoms-subscale (AUC=0.802)

Conclusion: Although frail OA patients have lower functioning scores at baseline, the change-scores on HOOS/KOOS-subscales are similar for both frail and non-frail patients.

Introduction

Osteoarthritis (OA) is a common, degenerative, disabling joint disease, affecting up to 23.1% of persons aged over 70 years.[2] These numbers are likely to increase due to population ageing and the epidemic proportions of obesity in the general population.[3,4] Thus far no cure for OA has been found; instead when pain relief is not sufficient anymore, the final treatment option is Total Joint Arthroplasty (TJA) in hip (THA) or knee (TKA). In the Netherlands, 28,798 THAs and 24,107 TKAs were performed in 2015 with up to 50% of the THA and 42% of TKA in persons aged ≥70.[5]

Despite these large numbers, about 10-20% of all THA and TKA patients are not satisfied with their post-operative results.[6,7] One of the reasons might be pre-operative state of the patient, reflected by frailty.

Frailty is a common syndrome in the elderly, with an overall prevalence of frailty amongst people aged ≥65 of 10.7%.[8,9] Frailty, as a representative of health and functional status, hampers the capacity to resist stressors, which in turn leads to increased susceptibility for adverse outcomes after surgery.[9-13] Reported levels of frailty vary greatly amongst age groups, with the pooled prevalence rates for persons aged between 65-69 being below 5% while for those aged 80-85 this is over 15% and even over 25% for persons aged ≥85.[8] Within persons of the same age group, substantial heterogeneity is present to the levels of frailty an individual might experience.[10,11,14-16]

Previously we have shown that the Groningen Frailty Indicator (GFI) is a feasible and validated questionnaire in persons with end stage hip or knee OA.[1] Using the GFI with a cut-off value of 4, we demonstrated that up to one third of the end stage OA-patients scheduled to undergo THA and a quarter of those scheduled for TKA are considered to be frail.[1]

Mandl *et al*[17] have addressed adverse events after TJA in 241 frail and non-frail patients and found that there was only an association between activities of daily life and adverse events after TJA. However, this study had a follow-up period of only 30 days and is not representative for the long-term functional outcome of TJA in patients

with end stage hip or knee OA. A study by McIsaac *et al*[18] (follow-up 1 year) in 125163 TJA-patients studied healthcare resource usage but not functional outcomes. They found frail patients to have increased mortality, increased length of stay in hospital, higher chance of re-admission and higher rates of discharge to institutional care after TJA as compared to non-frail TJA patients. A study on the impact of frailty on the long-term postoperative function has, to our knowledge, not yet been performed.

In this study, we aim to assess whether frail persons (cut-off value GFI≥4) have lower gain in post-operative function and quality of life. We also assess by means of ROC-curves whether the pre-operative GFI is valuable tool to discriminate between THA and TKA with high (good) and low (adverse) gain in function at one-year post-operative.

Methods

This analysis was performed in the longitudinal prospective cohort study *"Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis Study (LOAS, Trial ID NTR3348)"* which consists of patients undergoing total hip or knee arthroplasty for primary osteoarthritis. Participants were selected from 7 participating hospitals (the Leiden University Medical Center, Leiden; Alrijne Hospital, Leiden/Leiderdorp (former Diaconessenhuis and Rijnland Hospital); Groene Hart Hospital, Gouda; LangeLand Hospital, Zoetermeer; Reinier de Graaf Gasthuis, Delft; Albert Schweitzer Hospital, Dordrecht; Waterland Hospital, Purmerend).

Patients

All TJA patients aged over 18 years able to complete questionnaires in Dutch were eligible for participation. Patients were excluded if the physical or mental status did not allow participation or in case they did not sign the informed consent. Written and oral information about the study was given by the treating medical specialist at the outpatient clinic. Patients willing to be approached by the researcher received additional written information about the study by regular mail or e-mail, as well as a questionnaire, a stamped return envelope and a consent form. Patients were included once written informed consent was obtained according to the Declaration of Helsinki.[19]

For the purpose of the present analysis only data from patients who returned both the preoperative and the 12 month follow-up questionnaires was included. Ethical approval was obtained from the Medial Ethics Committee of the Leiden University Medical Center (registration number P12.047) and funding was received from the Dutch Arthritis Foundation (LLP13).

Assessments

Demographic variables: The collected socio- and demographic characteristics of the patients included: age (years); sex and length (cm) and weight (kg) to calculate the Body Mass Index (BMI). Living situation was also collected and divided in 'living alone' or 'living together', the latter category included persons living with family members as well as persons living in community housing.

Comorbidities: The presence of comorbidities was assessed by means of a self-reported questionnaire comprised of 19 different comorbidities. Patients were asked to respond with either yes or no to the question “Have you received any treatment for [disease] in the past year”. The included diseases were then clustered in two groups: musculoskeletal comorbidities (severe back pain, severe neck or shoulder pain, severe elbow wrist or hand pain, inflammatory arthritis or other joint conditions) or other comorbidities (asthma or COPD, cardiac disorder or coronary disease, arteriosclerosis, hypertension, stroke, severe bowel disorder, diabetes mellitus, migraine, psoriasis, chronic eczema, cancer and urine incontinence, hearing or visual impairments and dizziness in combination with falling).

Groningen Frailty Indicator: The presence of frailty was analysed by means of the Groningen Frailty Indicator (GFI). The GFI is a 15 item validated questionnaire based on many aspects of life: activities of daily life, medication use, mental state, vision and hearing. Each item can give one point, resulting in a maximum score of 15. A patient with a score of ≥4 was considered frail.[20-23] The GFI has been validated to be used in patients with end-stage OA scheduled to undergo arthroplasty surgery.[1]

Functional outcome (HOOS/KOOS): Patient function was assessed by the validated Hip disability/Knee injury Osteoarthritis Outcome Score (HOOS/KOOS) questionnaires for hip and knee patients respectively. Both questionnaires comprise five domains: activities of daily living (ADL), quality of life (QoL), sports (SP), symptoms (SYM) and pain (P).[24,25] For the current study the validated Dutch versions of the HOOS/KOOS were used.[26,27]

Statistical analyses

Demographic characteristics of frail and non-frail patients were compared for hip and knee arthroplasty separately by means of Student's T-test (continue, normally distributed variables), Mann-Whitney U-test (continue, not normally distributed variables) or Chi-square (categorical variables), whichever was appropriate; per joint site.

Functional outcomes were assessed by means of the 5 subscales of the HOOS/KOOS questionnaire (pain (P), symptoms (S), activity limitations of daily living (A), sport and recreation functioning (SP) and joint related quality of life (QoL)). Scores were compared between frail and non-frail patients by means of Mann-Whitney U-test for each time point (baseline and 12 months) separately. In addition, for each of these scores a change-score was calculated by subtracting pre-surgery score from the 1-year follow-up scores. These were compared between frail and non-frail patients (cut-off value GFI≥4) by means of Mann-Whitney U-test.

Adverse outcome was defined as improving less than twice the Minimal Clinically Important Difference (MCID), meaning an improvement of less than 20 points on the HOOS/KOOS in the year after surgery.[24] This binary score (more or less than twice MCID) was calculated for each subscale of the HOOS/KOOS. For each subscale a logistic regression model was estimated with the binary outcome score and GFI as continue independent risk factor (Model1). Then a multivariable logistic regression model with GFI and baseline HOOS/KOOS score as prognostic factor was estimated (Model 2). Finally, a univariate logistic regression model was estimated to assess the association of baseline HOOS/KOOS score on GFI (Model 3). AUC was estimated to assess the discriminatory ability of the logistic regression models.[28]

All analyses were performed separately for THA and TKA patients. Data were analysed using the SPSS statistical package (version 20.0, SPSS, Chicago, Illinois). The level of statistical significance was set at $P \leq 0.05$ for all analyses.

Results

Among the 3,190 patients that were included in the LOAS-cohort, 1,570 (873 THA and 697 TKA) completed the HOOS/KOOS questionnaires at baseline and at 12 months follow-up. Of these, 92% also completed the GFI, resulting in 1445 persons in our analyses (805 THA and 640 TKA), see also Figure 1. Patients who did not complete the GFI were significantly older than those who did (mean (SD) age in years completed 66 (9.1), mean (SD) age not completed 69 (8.6), P=0.008) and female (72.8% female not completed, 63.5% female completed, P=0.04). No significant differences for BMI, musculoskeletal or other comorbidities were observed.

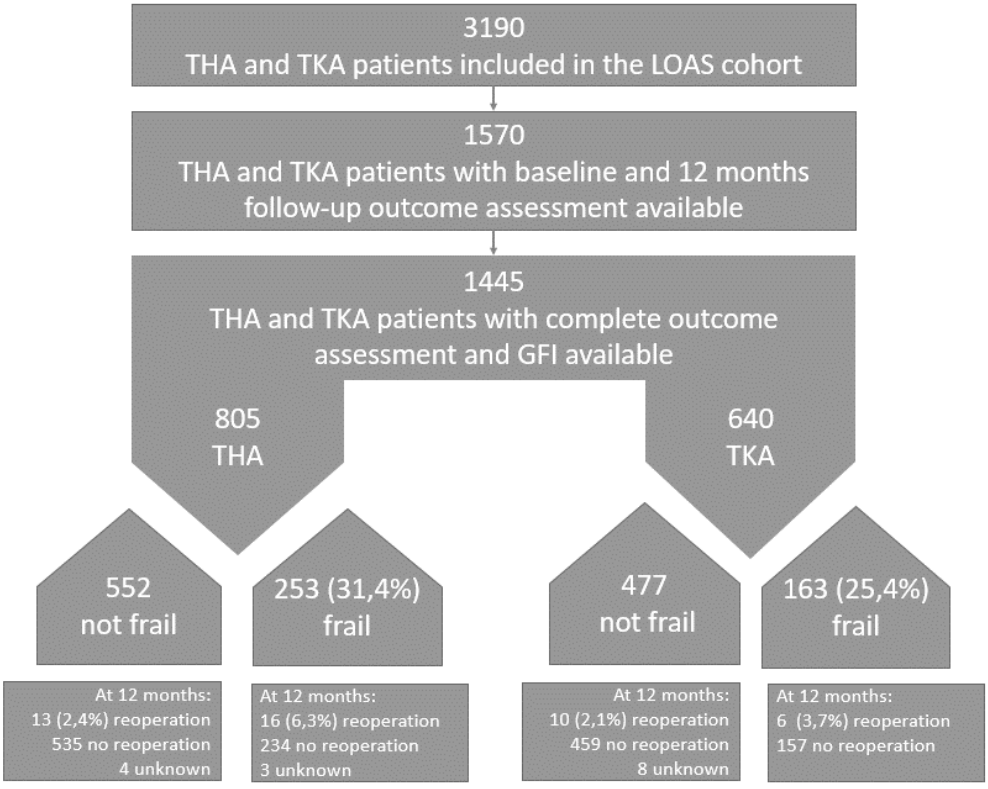

Figure 1 – Flowchart of patients included in the study and their final outcome.

Upon comparing frail patients to non-frail patients, significant differences were found for almost all the socio-demographic characteristics included in the analyses. Frail persons were more often female, older, had more comorbidities, a higher BMI and were more often living alone as compared to non-frail end-stage hip or knee OA patients (see also Table 1). Within the group of frail patients, frail patients with knee OA had significant higher BMI as compared to frail hip OA patients (results not shown).

Table 2 shows the crude baseline and the 12-month follow-up scores on each of the HOOS/KOOS subscales as well as the change score. Except for the KOOS-symptoms subscale, all baseline and 12 months scores of the HOOS/KOOS subscales were statistically significantly different in the frail persons as compared to non-frail patients. However, the significant difference between frail and non-frail is only clinically relevant at baseline in the subscale pain for hip and subscale ADL for both hip and knee. At 12 months the MCID-threshold of 10 is only reached in ADL for hip patients and in the subscale sports for hip and knee patients.[24]

Table 1 - Demographic characteristics of frail and non-frail (as defined by the Groningen Frailty Indicator (GFI)) end-stage osteoarthritis patients.

	Hip					Knee				
	Non-Frail		Frail (GFI≥4)			Non-Frail		Frail (GFI≥4)		
	N=552		N=253		P*	N=477		N=163		P*
Female N(%)	312	56.5%	187	74.2%	<0.001	291	61.5%	125	76.7%	<0.001
Age mean (SD)	66.2	9.1	68.3	10.3	0.004	66.1	8.6	68.2	8.7	0.010
BMI mean (SD)	26.6	3.8	28.1	5.3	<0.001	28.9	4.4	30.0	5.2	0.022
MSK comorb[A] N(%)	64	12.0%	60	25.0%	<0.001	98	21.6%	44	29.3%	0.054
Other comorb[B] N(%)	321	65.0%	185	84.1%	<0.001	294	70.5%	117	84.2%	0.001
Living alone N(%)	66	12.0%	88	34.8%	<0.001	78	16.4%	66	40.5%	<0.001

*P-value corresponding to Chi-square (discrete variables) or t-test (normally distributed continue variables) for differences between frail and non-frail persons within joint-specific group.

A MSK cormob. - Musculoskeletal comorbidities include severe back pain, severe neck or shoulder pain, severe elbow wrist or hand pain, inflammatory arthritis or other joint conditions.

B Other comorb _ Other comorbidities include asthma or COPD, cardiac disorder or coronary disease, arteriosclerosis, hypertension, stroke, severe bowel disorder, diabetes mellitus, migraine, psoriasis, chronic eczema, cancer and urine incontinence, hearing or visual impairments and dizziness in combination with falling.

Table 2 - Baseline and change scores of the HOOS/KOOS subscales at 12 months.

		Hip					Knee				
		Non-Frail		Frail (GFI≥4)		P-value*	Non-Frail		Frail (GFI≥4)		P-value*
		Mean	SD	Mean	SD		Mean	SD	Mean	SD	
Pain	Baseline Score	40.9	17.9	30.9	17.8	<0.001	41.0	17.1	33.6	17.5	<0.001
	12 month Score	89.8	15.4	82.3	20.9	<0.001	87.5	17.3	81.1	19.0	<0.001
	Change Score	48.8	20.6	51.6	24.1	0.068	46.7	21.6	47.6	23.3	0.713
Symptoms	Baseline Score	41.4	18.5	35.2	17.3	<0.001	44.3	12.9	41.9	13.6	0.058
	12 month Score	82.7	18.6	73.0	20.5	<0.001	57.1	12.6	55.5	13.6	0.257
	Change Score	41.3	23.1	37.8	24.5	0.057	12.9	16.1	13.6	16.3	0.768
ADL^	Baseline Score	43.8	18.7	31.3	17.9	<0.001	48.8	17.0	37.8	17.8	<0.001
	12 month Score	87.5	15.7	76.7	22.0	<0.001	85.9	16.4	77.7	19.3	<0.001
	Change Score	43.7	20.5	45.4	24.5	0.261	37.1	19.9	39.9	22.6	0.136
Sports	Baseline Score	21.1	19.6	11.6	14.7	<0.001	11.3	14.2	7.4	12.5	<0.001
	12 month Score	70.5	25.0	54.3	29.0	<0.001	47.7	27.9	35.3	29.0	<0.001
	Change Score	49.4	27.9	42.6	29.9	0.002	36.4	26.7	27.9	27.7	<0.001
QoL$	Baseline Score	34.2	10.5	31.7	9.6	0.003	35.3	10.5	32.4	9.7	0.001
	12 month Score	60.5	15.7	56.1	18.3	0.003	54.4	16.3	48.5	15.4	<0.001
	Change Score	26.3	16.6	24.5	19.7	0.188	19.1	17.8	16.1	15.5	0.020

Scores of the HOOS/KOOS subscales at baseline and at 12 months. Included are also the change scores.

* Differences between frail and non-frail patients assessed by means of Mann-Whitley's test for non-parametric distributions.

^ ADL - Activities of Daily Life subscale of the HOOS/KOOS questionnaire

$ QoL - Quality of Life subscale of the HOOS/KOOS questionniare

The change-score for the Sports subscale was lower in frail as compared to non-frail in both hip (P=0.002) and knee (P<0.001). Also for the Quality of Life-subscale in knee a lower outcome change-score was found for frail persons (P=0.02). This suggests that the development over time, i.e. the change-score, in most subscales is similar in frail and non-frail persons. Only in Sports and QoL, non-frail persons have a more rapid increase in functioning after arthroplasty.

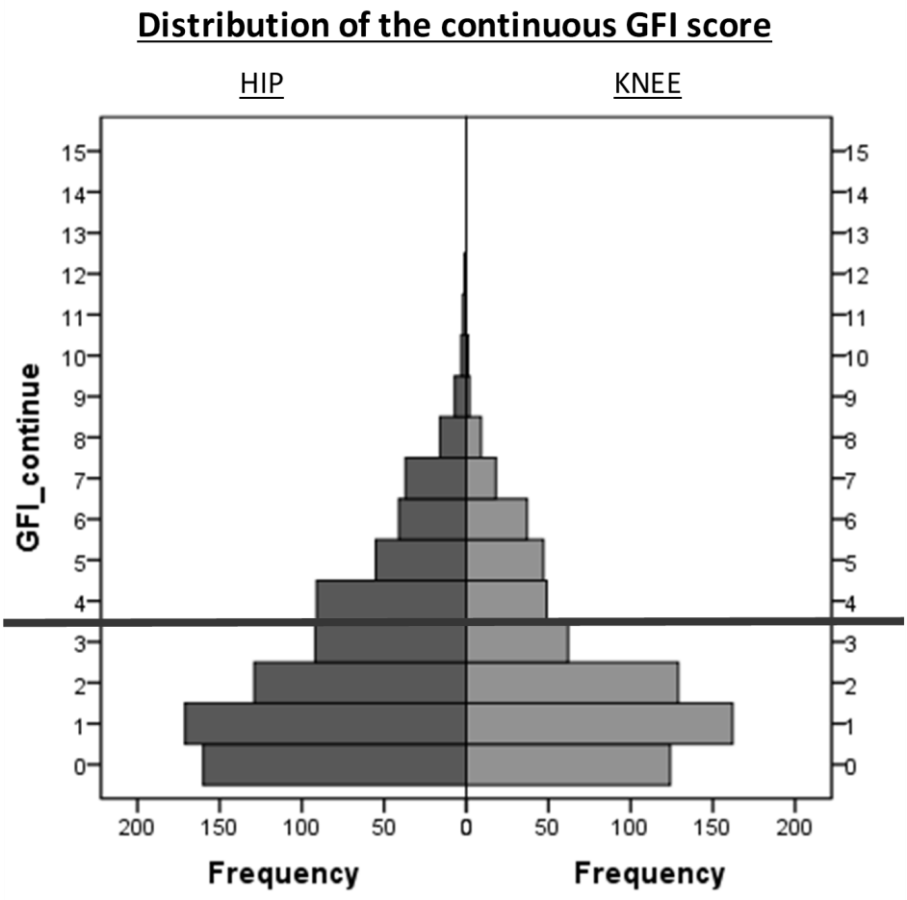

Figure 2 - Distribution of the Groningen Frailty Indicator (GFI) scores (range 0-15) stratified for affected joint.

Using the continuous scores of GFI (range 0-15, Figure 2); the potential of the GFI to discriminate between outcomes was assessed by constructing three models and the AUC for each model was estimated (Table 3). The model that included only GFI had poor discriminatory value (maximum AUC was 0.643 for Sports subscale in THA). The AUC for the model with GFI and baseline score as risk factors was equal to 0.804 for Symptoms in TKA while the model with only baseline score as risk factor had an AUC equal to 0.802 for Symptoms in TKA (Table 3).

Finally, we assessed the number of reoperations that were performed in the first 12 months post primary hip or knee arthroplasty and compared the rates of frail to the rate in the non-frail patients (Figure 1). Of the 163 frail patients with a knee replacement, 6 (3.7%) had to be re-operated on the same knee within 12 months, this rate was lower in the non-frail knee patients (2.1%, P=0.278). For persons with a hip replacement we did see a significant lower rate of re-operations in the non-frail patients (2.4%) as compared to the frail patients (6.4% P=0.005).

Table 3 – Discriminatory power between more or less than twice the MCID increase for various models in- and excluding Groningen Frailty Indicator (GFI).

	Hip			Knee		
	Model 1[A]	Model 2[B]	Model 3[C]	Model 1[A]	Model 2[B]	Model 3[C]
Pain	0.498	0.712	0.697	0.543	0.730	0.705
Symptoms	0.549	0.797	0.767	0.510	0.804	0.802
Activities of Daily Life	0.532	0.795	0.753	0.539	0.734	0.708
Sport	0.643	0.705	0.573	0.588	0.597	0.557
Quality of Life	0.575	0.623	0.623	0.561	0.611	0.582

Area under the estimated ROC curve corresponding to different models.
A - Model 1: Univariate analysis with Groningen Frailty Indicator (GFI) score as prognostic factor.
B - Model 2: Multivariate analysis with GFI and baseline score as prognostic factor.
C - Model 3: Univariate analysis with baseline score as prognostic factor.

Discussion

Although obvious preoperative (i.e. baseline) differences in values for the HOOS/KOOS subscales existed between frail and non-frail patients who undergo TJA, frailty did not discriminate between good or adverse outcome.

A model for TKA including GFI and pre-operative Symptoms-baseline score has an AUC equal to 80.4% for distinguishing between patients with a twofold MCID change on the symptoms subscale of the HOOS/KOOS. When only the pre-operative score was used, a similar AUC was found (80.2%), indicating that frailty has only a marginal additional value to increase this discriminatory value of post-surgery outcome in THA and TKA patients.

One reason might be the presence of selection bias, since only persons who are scheduled to undergo arthroplasty were included. This also explains skewed distribution of the continuous GFI scores. These persons have all undergone selection by the orthopaedic surgeon and those not considered fit to have surgery were excluded. The levels of frailty in this rejected group were unknown. However, amongst those undergoing surgery still 31.4% in hip and 25.4% in knee are considered frail by GFI (cut-off value of 4). Another problem may be the selection bias which is induced by excluding patients who, based on their mental or physical status, could not complete the questionnaires. Exactly these patients may be those who are most frail. Unfortunately, we did not have data to assess exactly how many patients were not capable to complete the questionnaires.

A study by O'Neill *et al*[29] demonstrated that the initial clinical impression by a physician of a patient is a useful screening tool to predict for mortality in patients undergoing major surgery. Also, a study conducted by Gerdhem *et al*[30] has demonstrated the subjective estimate of physicians of biological age is appropriate. Our results support these studies in the sense that improving outcome within the current selection of the physician, who apparently allowed GFI-indicated frail patients, is not possible by GFI since both frail and non-frail profited almost equally from the operation.

In our study we did find that persons who are considered frail by GFI have more often comorbidities and higher BMI, however, this is not a strong prognostic factor for postoperative functional outcomes. This might be due to selection bias by the treating orthopaedic surgeon (i.e. more severe comorbid patients or patients with even higher BMI were not selected). However, our results are in line with a study in head and neck cancer patients, showing that frailty as measured by the GFI is not predictive for postoperative complications after surgery.[31] In contrast, a study by Baitar *et al*[32] found that GFI is able to separate patients with cancer with normal and abnormal Comprehensive Geriatric Assessment.

We did find a higher reoperation rate in the frail patients as compared to the non-frail patients, confirming previous studies that found that frailty is a predictor for adverse events such as complications, readmission and reoperation.[33-35] This could be related to the increased number of comorbidities as we saw in our frail population; however, this should be further assessed in future studies.

For functional recovery after arthroplasty surgery, we have now shown that GFI is not a strong prognostic factor. We found that the functional baseline score is a strong prognostic score which can fairly well discriminate between good and adverse functional outcomes. In addition, we found that frail persons have significant lower functional baseline scores than non-frail persons. Therefore, baseline score seems a better measurement to give any indication about the to-be-expected outcome of surgery over frailty score when focusing on functionality, not necessarily when focusing on QoL or health care use. Jiang *et al*[33] have also identified that worse baseline scores of OKS are associated with worse post-surgery OKS up to 10 years after TKA. Exploring what other health assessments apart from functional parameters would predict post-surgery functionality, such as metabolic and inflammatory conditions at baseline, might improve patient-specific outcome prediction.

The cut-off of more or less than twice the MCID to assess the effect of GFI was arbitrarily, however, if we set the threshold at once the MCID (i.e. 10-point increase) similar results were found.

A limitation of this study is the aforementioned selection bias, as we only assessed persons selected by their treating surgeon to undergo surgery and did not have information of patients who were not selected to undergo surgery. These latter patients are most likely to be frail. Nevertheless, up to one-third of the patients who do undergo surgery are considered frail as measured by the GFI.

Among the patients selected for THA and TKA, baseline frailty assessed by the GFI did not provide added value in distinguishing between patients with more or less than twice the MCID change on functional outcome score by the HOOS/KOOS index, one year post-operative. Theoretically, it may be possible that more frail patients, currently not admitted to surgery, would profit functionally from THA/TKA surgery. However, as we do see higher reoperation rates in the frail patients, further research is needed before broadening the indication for arthroplasty surgery.

We conclude that although frail OA patients have lower functioning scores at baseline, the change-scores on HOOS/KOOS-subscales are similar for both frail and non-frail patients.

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