

Predicting Functional Recovery and Quality of Life in Older Patients Undergoing Colorectal Cancer Surgery: Real-World Data From the International GOSAFE Study

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ABSTRACT

PURPOSE The GOSAFE study evaluates risk factors for failing to achieve good quality of life (QoL) and functional recovery (FR) in older patients undergoing surgery for colon and rectal cancer.

METHODS Patients age 70 years and older undergoing major elective colorectal surgery were prospectively enrolled. Frailty assessment was performed and outcomes, including QoL (EQ-5D-3L) recorded (3/6 months postoperatively). Postoperative FR was defined as a combination of Activity of Daily Living ≥ 5 + Timed Up & Go test <20 seconds + MiniCog >2.

RESULTS Prospective complete data were available for 625/646 consecutive patients (96.9%; 435 colon and 190 rectal cancer), 52.6% men, and median age was 79.0 years (IQR, 74.6–82.9 years). Surgery was minimally invasive in 73% of patients (321/435 colon; 135/190 rectum). At 3–6 months, 68.9%–70.3% patients experienced equal/better QoL (72.8%–72.9% colon, 60.1%–63.9% rectal cancer). At logistic regression analysis, preoperative Flemish Triage Risk Screening Tool ≥ 2 (3-month odds ratio [OR], 1.68; 95% CI, 1.04 to 2.73; $P = .034$, 6-month OR, 1.71; 95% CI, 1.06 to 2.75; $P = .027$) and postoperative complications (3-month OR, 2.03; 95% CI, 1.20 to 3.42; $P = .008$, 6-month OR, 2.56; 95% CI, 1.15 to 5.68; $P = .02$) are associated with decreased QoL after colectomy. Eastern Collaborative Oncology Group performance status (ECOG PS) ≥ 2 is a strong predictor of postoperative QoL decline in the rectal cancer subgroup (OR, 3.81; 95% CI, 1.45 to 9.92; $P = .006$). FR was reported by 254/323 (78.6%) patients with colon and 94/133 (70.6%) with rectal cancer. Charlson Age Comorbidity Index ≥ 7 (OR, 2.59; 95% CI, 1.26 to 5.32; $P = .009$), ECOG ≥ 2 (OR, 3.12; 95% CI, 1.36 to 7.20; $P = .007$ colon; OR, 4.61; 95% CI, 1.45 to 14.63; $P = .009$ rectal surgery), severe complications (OR, 17.33; 95% CI, 7.30 to 40.8; $P < .001$), fTRST ≥ 2 (OR, 2.71; 95% CI, 1.40 to 5.25; $P = .003$), and palliative surgery (OR, 4.11; 95% CI, 1.29 to 13.07; $P = .017$) are risk factors for not achieving FR.

CONCLUSION The majority of older patients experience good QoL and stay independent after colorectal cancer surgery. Predictors for failing to achieve these essential outcomes are now defined to guide patients' and families' preoperative counseling.

ACCOMPANYING CONTENT

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Appendix

Protocol

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INTRODUCTION

The goal of surgical management of older patients with colorectal cancer should be treating the malignancy while maintaining patients' quality of life and independence. Treatment plans should be made after multidisciplinary discussion in accordance with technical feasibility, the patient's goals, and

accurate fitness assessment. These cornerstones will offer the most suitable treatment option for the individual patient, which should not be based on chronologic age.^{1,2}

Surgeons have recently realized that some of the traditional oncologic outcomes (progression-free survival, disease-free survival, etc) have a limited value for senior patients whose

CONTEXT

Key Objective

Can older patients' quality of life (QoL) and functional recovery (FR) be restored after major cancer surgery? What are the risk factors for failing these?

Knowledge Generated

The majority of older patients experience a restored QoL and FR 3 months after colorectal cancer surgery. Pieces of information that are often neglected from routine patient evaluations are risk factors for failing at achieving a good QoL/FR. Those could be easily obtained with a frailty screening that can fit into everyday surgical practice. Postoperative complications determine a worse QoL/FR for a longer time than we previously thought. This should prompt surgeons to ponder the choice of a surgical strategy as the less stressful surgery could both promote a reduction in mortality and an increase in the chance of maintaining QoL/FR. All these previously unveiled items and their correlation with the restoration of QoL and function can help guide the conversation about possible surgical strategies.

Relevance (A.H. Ko)

This study provides reassurance that most older individuals are able to recover well after colorectal cancer surgery, while also highlighting the importance of screening for frailty measures that may predict for worse functional and QoL outcomes.*

*Relevance section written by JCO Associate Editor Andrew H. Ko, MD, FASCO.

primary target is to survive the surgery, regain independence, and enjoy a satisfactory postoperative quality of life (QoL).^{3,4}

The GOSAFE (Geriatric Oncology Surgical Assessment and Functional rEcovery after Surgery) study has been specifically designed to shed light on outcomes that matter to patients in the real world. It was promoted by a multidisciplinary group sponsored by the European Society of Surgical Oncology and the Surgical Task Force of the International Society of Geriatric Oncology.

The overall results of the study population (1,005 patients) affected by different cancer types have been published.⁵ Hereby, we report on a homogeneous subgroup of patients affected by colon or rectal cancer.

The primary outcome was to clarify if patients' QoL could be restored to baseline after major cancer surgery in older patients with colon or rectum cancer.

The secondary end point was to identify a correlation between patients' status, including frailty assessments, with patient-reported outcomes (PROs) and functional recovery (FR) to shift patients' care toward personalized treatment while improving traditional clinical outcomes.

METHODS

The GOSAFE study is a multicenter, international prospective observational cohort study conducted at 26 hospitals worldwide (Appendix Table A1 [online only]). This study, registered

at ClinicalTrials.gov (identifier: [NCT03299270](https://clinicaltrials.gov/ct2/show/study?term=NCT03299270)) was approved by each center's institutional review board and ethics committee. Informed consent was obtained by each patient enrolled in the study.

Inclusion Criteria

All consecutive patients age 70 years and older undergoing elective major colorectal surgery with curative or palliative intent were eligible. Primary procedures (ie, any resection for colon or rectal cancer via any operative approach) were included to retrieve information on real-life practice; cognitive impairment was not considered an exclusion criterion. Patients not deemed surgical candidates by the single centers were not enrolled in the study and, therefore, data were not collected on these patients.

Exclusion Criteria

Patients undergoing emergent/urgent surgery or planned hospital stay <48 hours were excluded. Centers failing to provide at least 20 consecutive cases were also excluded.

The primary outcome was the comparison of QoL data before and after colorectal surgery (3 and 6 months). The EQ-5D-3L, a previously described and internationally validated tool, was used to measure QoL (Appendix Fig A1 [online only]).^{6,7} The EQ-5D-3L test results are presented in the form of an index and a visual analogue scale (VAS).

The index is based on patients' satisfaction in five domains (5D: mobility, self-care, ability to perform usual activities,

pain/discomfort, and anxiety/depression) across three levels (3L: no problem, some problems, and extremely problematic). On the basis of the scoring of all five domains and through an algorithm that converts individual patients' answers into a global index, a score is calculated ranging from 0 (poorest QoL) to 1 (best possible QoL). It was previously demonstrated that an increment of 0.13 in the EQ-5D-3L index is the minimal clinically important difference, including in the geriatric oncology population.⁸ To help the reader better understand the clinical relevance of the variation in the EQ-5D-3L index, this is reported as a post hoc threshold, but it was not used to dichotomize variables during the study. The VAS score of the EQ-5D-3L is generated by asking the patient how he/she ranked his/her QoL, compared with his/her peers, on a scale from 0 to 100. The value set generated from the European population (EQ) was used as the reference cohort.⁹

EQ-5D-3L is easy and quick to implement in any busy clinic; it has been validated by several studies^{10,11} including patients with cognitive disorders.¹²

The secondary outcomes include (1) defining if patients experienced FR after major colorectal cancer surgery and (2) defining which risk factors and frailty assessment tools were associated with QoL and FR.

FR at 3 and 6 months after surgery was defined as a combination of three outcomes: independence in the Activity of Daily Living (ADL ≥ 5)¹³ + The Timed Up & Go (TUG) test < 20 seconds¹⁴ + MiniCog > 2 .¹⁵ Vice versa, if patients were independent/functional on the combination of these 3 parameters before surgery but at least one of them was deranged at 3 or 6 months, the patient was considered functionally declined. The only exception was made if a patient was already dependent in one category before surgery and the same one was still deranged at 3 or 6 months; that patient was considered functionally stable and thus recovered.

The selection of frailty screening tools and their cutoffs was based on the evidence from the literature and previous experience from the research consortium.^{16,17} Frailty screening was performed using The Eastern Collaborative Oncology Group performance status,¹⁸ Katz Activities of Daily Living (ADL),¹³ Flemish version of the Triage Risk Screening Test (fTRST),^{19,20} Timed Up & Go (TUG) test,¹⁴ the Geriatric 8 (G8),²¹ the Nutritional Risk Screening,²² American Society of Anesthesiologists (ASA) score,²³ and Charlson Age Comorbidity Index (CACI).²⁴ Specifics about frailty screening tests and perioperative assessment were previously reported (Appendix Table A2 [online only]).¹⁶

The baseline evaluation and postoperative follow-up assessments take approximately 20 minutes to complete; they were carried out by health care providers in the outpatient clinic as part of the routine perioperative evaluation.²⁵ No formal prehabilitation protocol was implemented and optimization was performed for individual patients on the

basis of the center's practice. Postoperative follow-up visits at 3 and 6 months allowed for measuring QoL and functional status. When a routine visit was not planned, an ad hoc in-person appointment or telephone interview was scheduled.

Postoperative morbidity was recorded according to the Clavien-Dindo classification (CD).²⁶ To maintain a homogeneous study population, patients with colon and rectal cancer were analyzed separately.

Centralized monitoring was conducted throughout the study conduction to maintain the highest possible data quality. Strengthening the Reporting of OBservational studies in Epidemiology reporting standards for cohort studies were strictly followed.

Statistical Analysis

Continuous variables were reported as median (IQR) or mean (SD). Categorical variables were reported by means of frequencies. McNemar test was used to evaluate change in the domains of EQ-5D-3L at 3/6 months after surgery and to test if the row and column marginal frequencies were equal when analyzing the relationship between QoL and FR. Primary outcome analysis for missing data was performed using a complete case analysis. A missing data analysis was conducted on patients without EQ-5D-3L data at 3 months: baseline QoL and frailty data were used to estimate EQ-5D-3L index at 3 months throughout multiple imputation analysis. No difference was observed between EQ-5D-3L index on complete-case data and the EQ-5D-3L index of the total of patients.

Patients who died before the 3-month evaluation were excluded from the QoL and FR data analysis.²⁷

Logistic regression analyses investigating the association of variables with the outcomes of worsened EQ-5D-3L index (yes/no) and failing to achieve FR (yes/no) at 3/6 months after surgery were performed. Crude and adjusted odds ratios (ORs) with 95% CIs were reported. A *P* value of $< .05$ was considered statistically significant.

Stepwise regression models starting with no predictor were carried out. Final models for QoL and lack of FR were chosen according to statistical appropriateness based on Akaike information criteria (AIC) and Bayesian information criteria (BIC) to limit the partial item overlapping from the frailty screening tools. Associations among frailty screening variables were explored through a stratified analysis and a test of homogeneity was carried out.

AIC and BIC were used for model comparison considering the fit and complexity of the models. Models with the lower BIC and AIC were superior for reporting the relationship between outcomes and risk factors. During the stepwise process,

when variables were found to be associated, the ones generating the model with the best BIC and AIC were selected.

The VAS score component of the EQ-5D-3L and the EQ-5D-3L index were considered continuous variables and an ANOVA for repeated measures was performed comparing preoperative versus 3-month versus 6-month results. Bonferroni's correction was used for post hoc comparisons. Linear mixed-effects models, which are robust to individual changes, were used to analyze EQ-5D-3L VAS score or EQ-5D-3L index as a dependent variable focusing on the main effect of time (baseline, evaluation at 3 months, and evaluation at 6 months) taking account for patient intravariability. All statistical analyses were carried out using Stata/MP 15.0 for Windows (StataCorpLP, College Station, TX).

RESULTS

Data obtained on 646 patients from 26 centers in the GOSAFE study group were prospectively collected from February 2017 to April 2019. A complete data set was obtained for 625 patients (435 with colon and 190 with rectal cancer). One patient had incomplete baseline data and 12 did not meet the inclusion criteria. Eight patients enrolled from centers that did not achieve the critical core volume were also excluded (Fig 1).

There were 329 men (52.6%) and the median age was 79.6 years (IQR, 74.6–82.9 years). The results of the frailty

screening tests and surgical characteristics are reported in Table 1. Frailty was reported in differing numbers of patients, depending on the frailty screening tool, fluctuating between 7.4% (ECOG >2) to 72.6% (G8 <14). Moderate to severe malnutrition was reported in 9.8% of patients and cognitive impairment in 23.3%.

Surgery was performed via a minimally invasive approach in 73.0% of patients (321/435, 73.8% colonic; 135/190, 71.1% rectal surgery). Among patients with rectal cancer, 35.3% (67/190) underwent a proctectomy with a permanent colostomy, 34.2% (65/190) a proctectomy (including total mesorectal excision [TME] or a partial mesorectal excision [PME]) with primary anastomosis, and 30.5% (58/190) a restorative proctectomy with a temporary ileostomy. Of this last group, 67.2% (39/58) had their ileostomy reversed during the following months (Table 1).

QoL data were available for 625 patients at baseline, 549 patients at 3 months (34 deceased before 3-month evaluation, 42 missing), and 538 patients at 6 months (23 lost to follow-up, 43 deceased, 21 missing). FR data were available for 456 and 461 patients at 3 and 6 months, respectively (Fig 1).

QoL Analysis

Data showed that 3 months after colon cancer surgery, the majority of patients reported stable or improved QoL

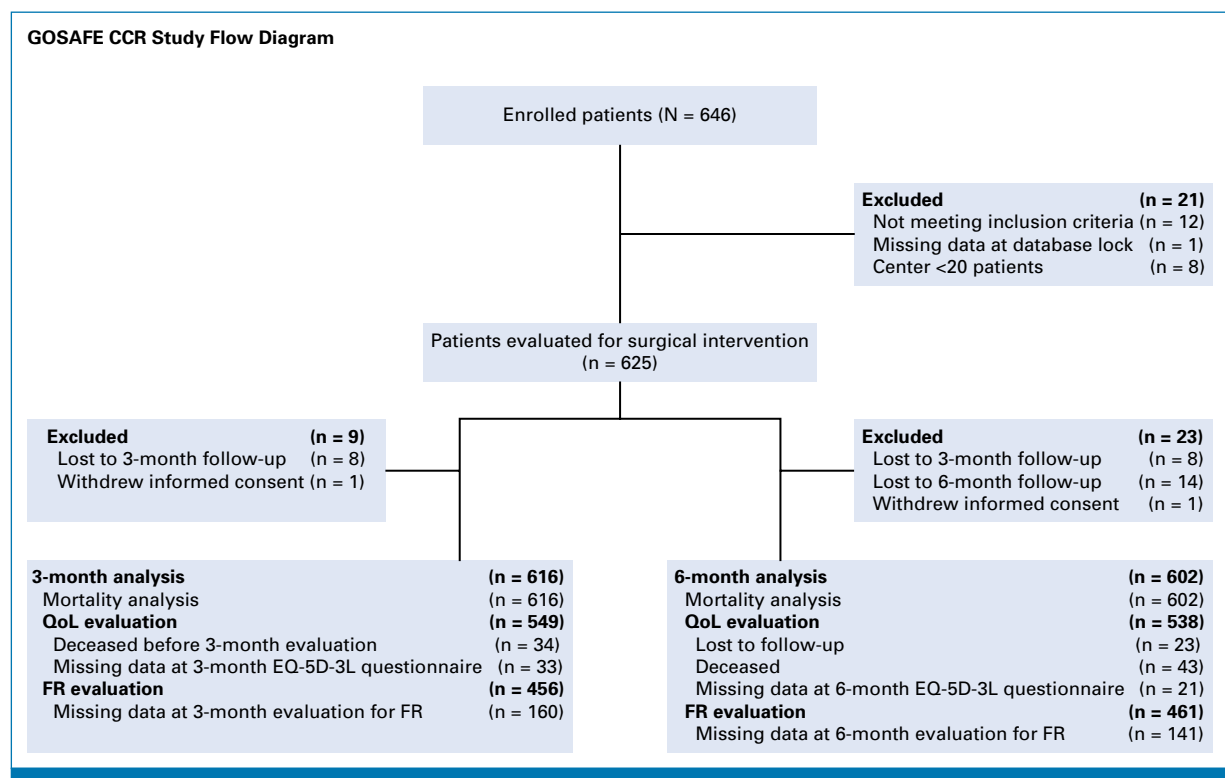


FIG 1. Study population flowchart showing the number of patients with a complete data set and patients who were excluded from the analysis because of incomplete data collection. FR, functional recovery; QoL, quality of life.

TABLE 1. Patient Baseline and Surgical Characteristics

Variable	Colon (n = 435)	Rectum (n = 190)	Total Patients (N = 625)
Sex, No. (%)			
Male	211 (48.5)	118 (62.1)	329 (52.6)
Female	224 (51.5)	72 (37.9)	296 (47.4)
Age, years, No. (%)			
70-74	120 (27.6)	56 (29.4)	176 (28.2)
75-79	117 (26.9)	63 (33.2)	180 (28.8)
80-84	124 (28.5)	48 (25.3)	172 (27.5)
≥85 years	74 (17.0)	23 (12.1)	97 (15.5)
Age, years			
Median (IQR)	79.6 (74.6-83.3)	78.4 (74.3-81.9)	79.0 (74.6-82.9)
Living situation, No. (%)			
Home-independent	238 (54.7)	76 (40.0)	314 (50.2)
Home with family/caregiver	192 (44.1)	111 (58.4)	303 (48.5)
Residential care	5 (1.2)	3 (1.6)	8 (1.3)
Medication use, No. (%)			
None	20 (4.6)	21 (11.1)	41 (6.6)
Drugs, No., median (IQR)	4 (2-6)	4 (2-6)	4 (2-6)
Missing	20	21	41
History of falls 6 months before operation, No. (%)	43 (9.9)	17 (8.9)	60 (9.6)
Previous delirium, No. (%)	25 (5.8)	10 (5.3)	35 (5.6)
Smoking habits, No. (%)			
Yes	32 (7.4)	23 (12.1)	55 (8.8)
No (former)	175 (40.2)	80 (42.1)	255 (40.8)
No (never)	228 (52.4)	87 (45.8)	315 (50.4)
ASA score, No. (%)			
1-2	213 (49.9)	90 (47.9)	303 (49.3)
3-4	214 (50.1)	98 (52.1)	312 (50.7)
Missing	8	2	10
CACI, No. (%)			
3-6	283 (65.1)	139 (73.2)	422 (67.5)
≥7	152 (34.9)	51 (26.8)	203 (32.5)
G-8 total score, No. (%)			
Median (IQR)	12.5 (11.0-14.0)	13.0 (11.0-15.0)	13.0 (11.0-15.0)
G-8 ≤14	329 (75.6)	125 (65.8)	454 (72.6)
G-8 >14	106 (24.4)	65 (34.2)	171 (27.4)
fTRST, No. (%)			
0	107 (24.6)	62 (32.6)	169 (27.0)
1	168 (38.6)	67 (35.3)	235 (37.6)
≥2	160 (36.8)	61 (32.1)	221 (35.4)
NRS, No. (%)			
Normal	259 (60.5)	117 (62.2)	376 (61.0)
Mildly impaired	126 (29.4)	54 (28.7)	180 (29.2)
Moderately impaired	32 (7.5)	15 (8.0)	47 (7.6)
Severely impaired	11 (2.6)	2 (1.1)	13 (2.2)
Missing	7	2	9
ADL score, No. (%)			
<5	38 (8.8)	23 (12.3)	61 (9.8)
≥5	396 (91.2)	164 (87.7)	560 (90.2)
Missing	1	3	4

(continued on following page)

TABLE 1. Patient Baseline and Surgical Characteristics (continued)

Variable	Colon (n = 435)	Rectum (n = 190)	Total Patients (N = 625)
MINICOG total score, No. (%)			
0-2	107 (24.9)	37 (19.7)	144 (23.3)
3-5	323 (75.1)	151 (80.3)	474 (76.7)
Missing	5	2	7
ECOG PS, No. (%)			
0	204 (46.9)	112 (59.0)	316 (50.6)
1	155 (35.6)	44 (23.2)	199 (31.8)
2	46 (10.6)	18 (9.5)	64 (10.2)
>2	30 (6.9)	16 (8.3)	46 (7.4)
TUG, No. (%)			
≤20	354 (90.3)	163 (89.1)	517 (89.9)
>20	38 (9.7)	20 (10.9)	58 (10.1)
Missing	43	7	50
Preoperative chemotherapy, No. (%)	13 (3.0)	66 (34.7)	79 (12.6)
Preoperative radiation therapy, No. (%)	13 (3.0)	74 (38.9)	87 (13.9)
Operative data			
Type of surgery, No. (%)			
Curative	411 (94.5)	178 (93.7)	589 (94.2)
Palliative	24 (5.5)	12 (6.3)	36 (5.8)
Type of anesthesia, No. (%)			
General	414 (95.2)	179 (94.2)	593 (94.9)
General + epidural	21 (4.8)	11 (5.8)	32 (5.1)
Duration of anesthesia, minutes, median (IQR)	180 (135-232)	260 (185-340)	192 (145-261)
Unknown	7	1	8
Surgical approach, No. (%)			
Open	114 (26.2)	54 (28.4)	168 (26.9)
Laparoscopic	315 (72.4)	120 (63.2)	435 (69.6)
Robotic	6 (1.4)	15 (7.9)	21 (3.4)
Other (excision trans anal)	0 (0.0)	1 (0.5)	1 (0.1)
Rectal cancer surgery, No. (%)			
APR	—	67 (35.3)	67 (35.3)
Proctectomy (PME + TME)	—	65 (34.2)	65 (34.2)
Proctectomy + ileostomy	—	58 (30.5)	58 (30.5)
Need of ICU stay, No. (%)	91 (21.0)	55 (29.1)	146 (23.4)
Days of ICU stay, No. (%)			
1	63 (69.2)	36 (65.4)	99 (67.8)
2	16 (17.6)	9 (16.4)	25 (17.1)
≥3	12 (13.2)	10 (18.2)	22 (15.1)
Blood transfusion, No. (%)	46 (10.6)	21 (11.1)	67 (10.8)
Discharge in the same preoperative setting, No. (%)	331 (76.3)	140 (74.1)	471 (75.6)
Patient transferred to medicine/rehabilitation facility, No. (%)	31 (7.1)	21 (11.1)	52 (8.4)
Postoperative nutritional supplement, No. (%)	93 (21.5)	64 (33.9)	157 (25.2)
Oral	43 (46.2)	32 (50.0)	75 (47.8)
Enteral	4 (4.3)	2 (3.1)	6 (3.8)
Parenteral	46 (49.5)	30 (46.9)	76 (48.4)
Presence of surgical complication	146 (33.8)	82 (43.4)	228 (36.7)
Chemotherapy postsurgery	93 (24.1)	43 (25.4)	136 (24.6)
Missing	49	21	70

Abbreviations: ADL, Katz Activities of Daily Living; APR, abdominoperineal resection; ASA, American Society Anesthesiologists; CACI, Charlson Age Comorbidity Index; ECOG PS, Eastern Collaborative Oncology Group performance status; fTRST, Flemish version of the Triage Risk Screening Test; G8, the Geriatric 8; ICU, intensive care unit; NRS, Nutritional Risk Screening; PME, partial mesorectal excision; TME, total mesorectal excision; TUG, Timed Up & Go.

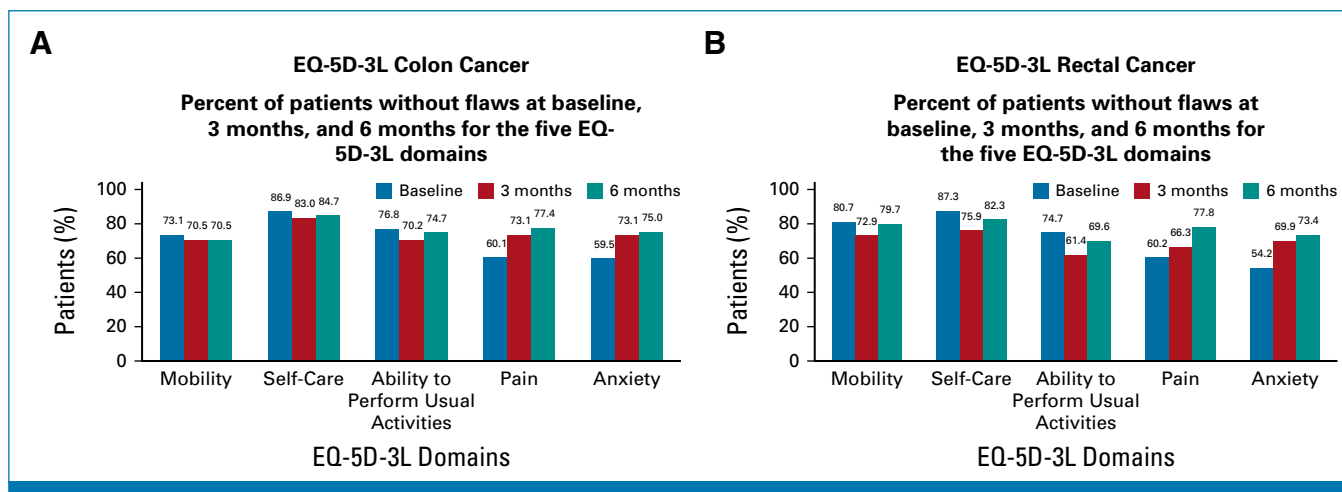


FIG 2. Quality of life after major (A) colon and (B) rectal cancer surgery. EQ-5D-3L single-domain analysis showing an immediate improvement of pain/discomfort and anxiety/depression. Three months after surgery, 69.0% (379/549 patients, 72.8% of those with colon and 60.2% with rectal cancer) of patients experienced equal or better quality of life according to the comprehensive EQ-5D-3L index.

according to the EQ-5D-3L compared with their preoperative status (Fig 2).

Three months after surgery, 69.0% (379/549 patients, 72.8% of those with colon and 60.2% with rectal cancer) of patients experienced equal or better quality of life according to the EQ-5D-3L index. After 6 months, 70.3% of patients reported equal or better results (72.9% of those with colon and 63.9% with rectal cancer).

EQ-5D-3L Index

Linear mixed-effect model, taking account of variability for individual patients, showed an effect of time over EQ-5D-3L index (beta coefficient = 0.618, P value < .001 for colon cancer; and beta coefficient = 0.592, P value < .001 for rectal cancer).

Repeated-measures analysis, on the basis of the EQ-5D-3L index, showed an improvement over time both for the colon and rectum subgroups (P value < .001). On the basis of the EQ-5D-3L index, QoL was even better 6 months after surgery.

For patients with colon cancer, a mean EQ-5D-3L index of 0.77 was observed at baseline (SD = 0.21) with an index of 0.82 at 3 months (SD = 0.21; P = .001 for post hoc comparison between baseline v 3 months) and this result is maintained at 6 months after surgery with a mean value of 0.83 (SD = 0.21; P < .001 for post hoc comparison among baseline v 6 months and P = .951 for post hoc comparison of 3 v 6 months). Patients with rectal cancer had a slower recovery in QoL, which was equal to 0.77 (from 0.78 at baseline, SD = 0.19) at 3 months (SD = 0.25; P = .635 for post hoc comparison of baseline v 3 months) and 0.82 at 6 months (SD = 0.23; P = .214, for post hoc comparison of baseline v 6 months and P = .009 for post hoc comparison of 3 v 6 months).

EQ-5D-3L VAS Score

Similar trajectories were recorded when analyzing the visual component of the EQ-5D-3L for patients with colon and rectal cancer. Mean VAS score was 69.7 (SD = 19.3) before surgery versus 72.7 (SD = 17.5) and 74.1 (SD = 17.0) at 3 and 6 months (P = .012 for post hoc comparison among baseline v 3 months and P < .001 for comparison among baseline v 6 months) for patients undergoing colectomy. Data were similar among 3 and 6 months (P value = .909). However, mean VAS scores were similar (P value for ANOVA = .166) before and after rectal cancer surgery, reporting a mean value equal to 68.9 (SD = 17.9) at baseline, 68.9 (SD = 19.1) at 3 months, and 71.9 (SD = 19.9) at 6 months.

Figure 2 demonstrates the fluctuation of EQ-5D-3L domains for the two groups. After 3 and 6 months, both pain/discomfort and anxiety/depression improved, with 73.1/77.4% and 73.1/75.0% of patients with colon cancer reporting no issues at 3/6 months (compared with 60.1% and 59.5% before surgery; P < .0001). Patients with rectal cancer reported an equivalent experience (no pain/discomfort in 66.3/77.8% of cases at 3-6 months v 60.2% at baseline and no anxiety/depression in 69.9/73.4% v 54.2% at baseline; P < .0001). Conversely, analysis of mobility, self-care, and ability to perform usual activities showed a lower level of satisfaction, although not statistically significant, after colonic surgery (73.1/86.9/76.8% before surgery v 70.5/83.0/70.2% at 3 months v 70.5/84.7/74.7 at 6 months). The gap between preoperative levels of satisfaction on these three items was more important for patients undergoing a proctectomy after 3 months, while the difference was mitigated after 6 months (80.7/87.3/74.7% at baseline v 72.9/75.9/61.4% at 3 months; P = .003; .005; .003; 79.7/82.3/69.6% at 6 months; P = .15; .058; .019, respectively).

Figure 3 shows the baseline and postoperative characteristics of those patients with colon and rectal cancer who

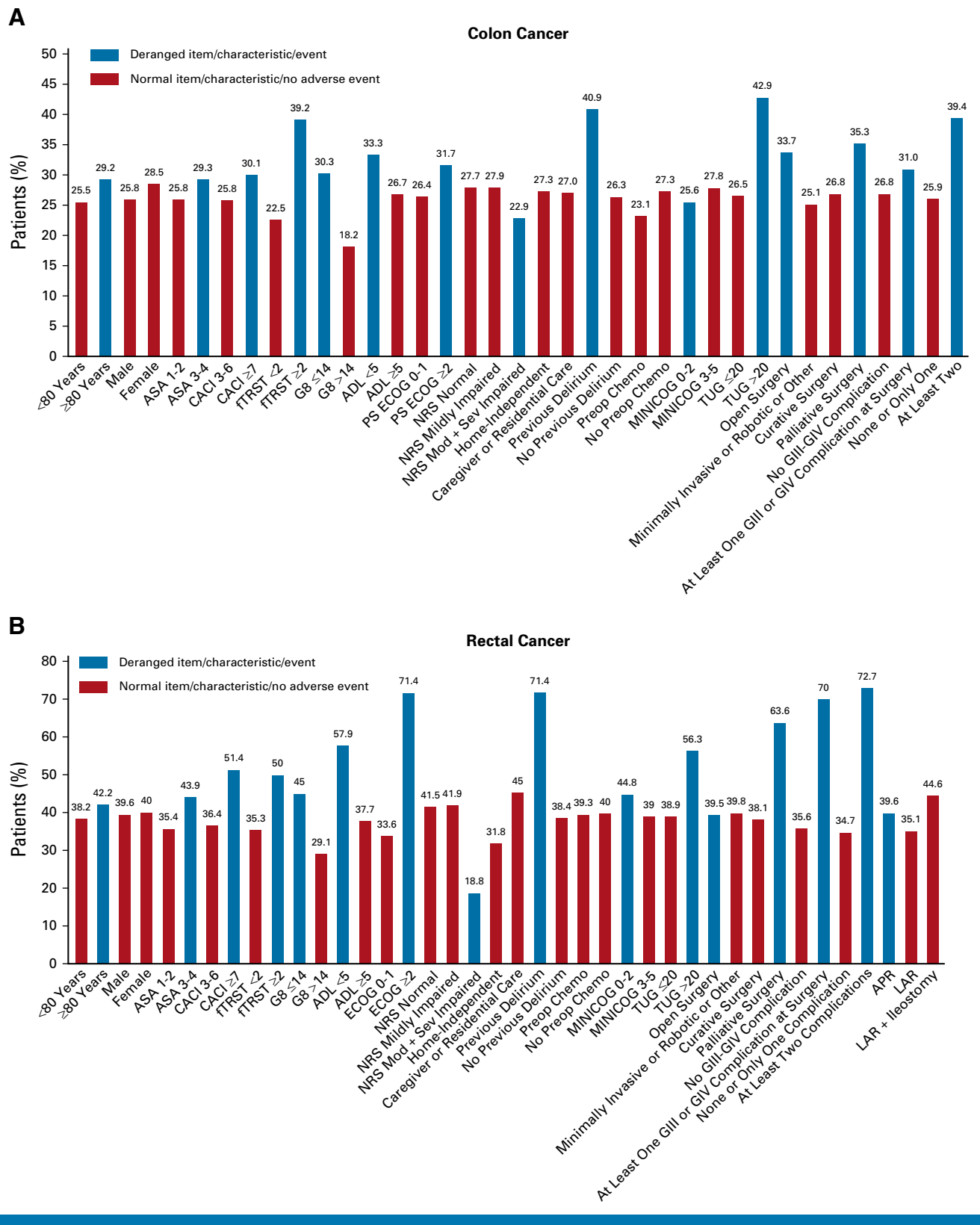


FIG 3. Baseline and postoperative characteristics of those patients with (A) colon and (B) rectal cancer who experienced worse QoL on the basis of the EQ-5D-3L index 3 months after surgery showing the relevant impact of frailty and postoperative complications on QoL restoration. ADL, activity of daily living; APR, abdominoperineal resection; ASA, American Society of Anesthesiologists; CACI, Charlson Age Comorbidity Index; chemo, chemotherapy; ECOG, Eastern Collaborative Oncology Group; fTRST, Flemish Triage Risk Screening Tool; G8, Geriatric 8; LAR, low anterior resection of the rectum; Mod, moderately; NRS, Nutritional Risk Screening; Sev, severely; TUG, Timed Up & Go.

experienced worse QoL on the basis of the EQ-5D-3L index, 3 months after surgery.

Logistic regression analysis was performed to identify risk factors for worsening QoL at 3 and 6 months for colon and rectal cancer separately. Among the two groups, patients were dichotomized into (1) patients who had a higher/equal postoperative EQ-5D-3L index than preoperative; and (2) patients who had a lower (worse) index postoperatively than preoperatively. Tables 2 and 3 report the univariable and multivariable analyses for patients with colon and rectal cancer. Logistic regression of the colon cancer subgroup shows that preoperative fTRST ≥ 2 is a risk factor associated with decreased QoL both at 3 and 6 months (OR, 1.68; 95% CI, 1.04 to 2.73; $P = .034$ and OR, 1.71; 95% CI, 1.06 to 2.75; $P = .027$, respectively). The same is found about the role of postoperative complications (OR, 2.03 for CDI-II complications; 95% CI, 1.20 to 3.42; $P = .008$ at 3 months; OR, 2.56 for CDIII-IV complication; 95% CI, 1.15 to 5.68; $P = .020$ at 6 months).

Logistic regression of the rectal cancer subgroup shows that preoperative ECOG ≥ 2 is a strong predictor for a postoperative drop in QoL at 3 months (OR, 3.81; 95% CI, 1.45 to 9.92; $P = .006$). In the 3-month analysis, patients with a severe complication or more than one complication (any grade) and palliative surgery (at the 6-month analysis) had a substantial impact but this was not statistically significant (OR, 2.85; 95% CI, 0.87 to 9.24; $P = .082$ and OR, 2.93; 95% CI, 0.88 to 9.72; $P = .079$; OR, 2.86; 95% CI, 0.92 to 8.94; $P = .070$, respectively).

The assumption that performing a restorative procedure in patients with rectal cancer is related to a better QoL was not supported by the statistical analysis as no difference in QoL was recorded between patients with or without an anastomosis at 3 or 6 months after surgery (OR, 0.82; 95% CI, 0.37 to 1.79; $P = .623$ and OR, 0.51; 95% CI, 0.19 to 1.32; $P = .163$, respectively, at 3 and 6 months).

Functional Recovery Analysis

Complete FR was reported by 254/323 (78.6%) patients with colon cancer and 94/133 (70.6%) with rectal cancer 3 months after major surgery with a minimal increment in the recovered population number after 6 months (+2, 256; and +4, 98 patients, respectively; Appendix Fig A2 [online only]).

Logistic regression of the colon cancer subgroup (Table 4) shows that preoperative CACI ≥ 7 and ECOG ≥ 2 are risk factors for failure to reach FR at 3 months (OR, 2.59; 95% CI, 1.26 to 5.32; $P = .009$; and OR, 3.12; 95% CI, 1.36 to 7.20; $P = .007$, respectively). Similarly, severe postoperative complications (CD III-IV) can affect the chance of FR (OR, 12.86; 95% CI, 4.67 to 35.44; $P < .001$ at 3 months; OR, 10.32; 95% CI, 3.76 to 28.33; $P < .001$ at 6 months). At 6 months, patients with fTRST ≥ 2 at baseline or who underwent palliative colonic surgery had a higher chance of not achieving FR (OR, 2.71;

95% CI, 1.40 to 5.25; $P = .003$; and OR, 4.11; 95% CI, 1.29 to 13.07; $P = .017$, respectively). In the 6-month analysis, patients who received minimally invasive surgery (MIS) experienced improved FR in a substantial amount of cases but this was not statistically significant (OR, 1.82; 95% CI, 0.93 to 3.55; $P = .080$, respectively).

Logistic regression in the rectal cancer subgroup (Table 5) shows that preoperative ECOG ≥ 2 is a strong predictor for failure to reach postoperative FR at 6 months (OR, 4.61; 95% CI, 1.45 to 14.63; $P = .009$), while no other variable was associated to 3- or 6-month FR.

Once again, the assumption that performing a restorative procedure in patients with rectal cancer would lead to a higher level of independence was not supported by the statistical analysis either at 3 or 6 months. Age was never associated with QoL or FR outcomes for patients with colon or rectal cancer.

Correlation Between QoL and FR Data

Possible overlaps between patients reporting better or improved QoL and those who experienced FR were analyzed. Appendix Table A3 (online only) shows a correlation between achieving a satisfactory QoL and FR at 3 and 6 months. Both 3- and 6-month analyses showed that the majority of patients have a positive relation between reporting a better/equal EQ-5D-3L index and FR. Similar numbers were reported at 3 months for patients with better/equal QoL and functional decline, as well as patients with worse QoL and FR (P value $> .05$). Conversely, in the 6-month analysis, there were a higher number of patients who recorded a poor QoL, but still experienced functional independence according to the study definition.

Although in the majority of cases a positive correlation between reporting a better/equal EQ-5D-3L index and FR was recorded, there were a number of patients, from 19.9% to 30.8% depending on the surgery/time, who recorded a poor QoL but still experienced functional independence according to the study definition.

The relation between the index and FR data also suggests that the perceived decline in mobility and ability to perform daily tasks (individually reported by the EQ-5D-3L and often scored by patients as diminished after surgery; Fig 2) is likely not substantial enough to prevent patients from being functionally independent.

DISCUSSION

To our knowledge, the GOSAFE real-world prospective data show, for the first time, that major colon and rectal surgery in older patients with cancer results in restoration of a good quality of life 3 and 6 months after surgery in the majority of cases. This demonstrates, together with the patients' ability

TABLE 2. Univariable and Multivariable Models for QoL at 3 and 6 Months (colon)

Covariates	3-Month QoL (N = 383)				6-Month QoL (N = 380)			
	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P	OR for Univariable Model (95% CI)	P	OR for Multivariable Model	P
Age ≥80 v <80 years	1.21 (0.77 to 1.89)	.410			1.01 (0.64 to 1.60)	.950		
Female v male	1.14 (0.73 to 1.80)	.551			1.33 (0.84 to 2.10)	.212		
ASA SCORE 3-4 v 1-2	1.19 (0.76 to 1.88)	.447			1.01 (0.64 to 1.59)	.950		
CACI ≥7 v 3-6	1.24 (0.77 to 1.99)	.376			1.33 (0.83 to 2.15)	.238		
fTRST ≥2 v <2	1.94 (1.22 to 3.10)	.005	1.68 (1.04 to 2.73)	.034	1.75 (1.10 to 2.79)	.018	1.71 (1.06 to 2.75)	.027
G-8 ≤14 v >14	1.95 (1.11 to 3.45)	.021	1.63 (0.91 to 2.95)	.103	1.48 (0.85 to 2.55)	.163		
ADL ≥5 v <5	0.72 (0.33 to 1.61)	.435			1.26 (0.49 to 3.24)	.627		
ECOG PS ≥2 v 0-1	1.29 (0.71 to 2.34)	.401			1.08 (0.58 to 2.04)	.799		
NRS mildly impaired v normal	1.01 (0.61 to 1.67)	.966			0.76 (0.45 to 1.30)	.322		
NRS moderately + severely impaired v normal	0.77 (0.33 to 1.79)	.548			1.03 (0.47 to 2.28)	.937		
Residential care or living with caregiver v home-independent	0.98 (0.62 to 1.55)	.954			0.64 (0.40 to 1.02)	.062		
Presence of delirium v absence	1.93 (0.80 to 4.68)	.141			1.86 (0.74 to 4.69)	.189		
Preoperative chemotherapy (yes v no)	1.25 (0.34 to 4.64)	.737			0.64 (0.18 to 2.23)	.487		
Positive screening for dementia v negative	0.89 (0.52 to 1.53)	.679			1.59 (0.94 to 2.67)	.078		
TUG ≥20 v <20	2.08 (0.95 to 4.58)	.069			1.33 (0.56 to 3.17)	.523		
Open surgery v minimally invasive	1.52 (0.91 to 2.52)	.107			0.99 (0.59 to 1.68)	.996		
Palliative v curative surgery	1.49 (0.53 to 4.14)	.443			3.80 (1.29 to 11.24)	.016	2.86 (0.92 to 8.94)	.070
Only CDI-II complication v none	2.18 (1.30 to 3.64)	.003	2.03 (1.20 to 3.42)	.008	1.08 (0.62 to 1.88)	.776	1.03 (0.59 to 1.79)	.924
At least CDIII-IV complication v none	1.54 (0.66 to 3.56)	.312	1.45 (0.62 to 3.38)	.390	2.81 (1.29 to 6.14)	.009	2.56 (1.15 to 5.68)	.020
Two or more complication v none or only one	1.86 (0.88 to 3.88)	.101			1.02 (0.45 to 2.26)	.977		

NOTE. Bold indicates statistically significant *P* values for multivariable models to highlight final results.

Abbreviations: ADL, Katz Activities of Daily Living; ASA, American Society Anesthesiologists; CACI, Charlson Age Comorbidity Index; ECOG PS, Eastern Collaborative Oncology Group performance status; fTRST, Flemish version of the Triage Risk Screening Test; G8, the Geriatric 8; NRS, Nutritional Risk Screening; OR, odds ratio; QoL, quality of life; TUG, Timed Up & Go.

TABLE 3. Univariable and Multivariable Models for QoL at 3 and 6 Months (rectum)

Covariates	3-Month QoL (N = 166)				6-Month QoL (N = 158)			
	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P
Age ≥80 v <80 years	1.18 (0.62 to 2.23)	.613			1.47 (0.76 to 2.86)	.253		
Female v male	1.01 (0.54 to 1.92)	.959			1.09 (0.55 to 2.12)	.807		
fTRST ≥2 v <2	1.83 (0.93 to 3.58)	.078			2.17 (1.07 to 4.37)	.030	1.87 (0.83 to 4.26)	.132
G-8 ≤14 v >14	1.99 (1.01 to 3.98)	.050	1.57 (0.74 to 3.31)	.235	1.54 (0.76 to 3.12)	.226		
ASA SCORE 3-4 v 1-2	1.43 (0.76 to 2.68)	.265			0.78 (0.41 to 1.51)	.468		
CACI ≥7 v 3-6	1.84 (0.88 to 3.85)	.105			1.10 (0.51 to 2.36)	.799		
NRS mildly impaired v normal	1.01 (0.492.08)	.969			1.97 (0.93 to 4.14)	.076		
NRS moderately + severely impaired v normal	0.33 (0.09 to 1.21)	.094			2.11 (0.74 to 6.02)	.161		
ADL ≥5 v <5	0.44 (0.17 to 1.16)	.097			0.30 (0.10 to 0.82)	.019	0.46 (0.13 to 1.55)	.210
ECOG PS ≥2 v 0-1	4.94 (2.02 to 12.08)	<.001	3.81 (1.45 to 9.92)	.006	1.84 (0.78 to 4.38)	.164		
Residential care or living with caregiver v home-independent	1.75 (0.91 to 3.36)	.091			0.69 (0.36 to 1.34)	.285		
Preoperative chemotherapy (yes v no)	1.03 (0.53 to 1.98)	.929			0.62 (0.32 to 1.23)	.175		
Presence of delirium v absence	4.01 (0.76 to 21.35)	.103			2.47 (0.53 to 11.43)	.249		
Positive screening for dementia v negative	1.27 (0.57 to 2.86)	.559			0.98 (0.42 to 2.29)	.965		
TUG ≥20 v <20	2.02 (0.71 to 5.73)	.186			3.00 (1.01 to 8.94)	.049	1.41 (0.34 to 5.91)	.631
Palliative v curative surgery	2.84 (0.79 to 10.14)	.106			1.45 (0.37 to 5.62)	.592		
Only CDI-II complication v none	1.63 (0.79 to 3.35)	.180	0.88 (0.38 to 2.07)	.777	0.81 (0.37 to 1.80)	.610	0.44 (0.16 to 1.19)	.106
At least CDIII-IV complication v none	4.95 (1.74 to 14.09)	.003	2.85 (0.87 to 9.24)	.082	3.55 (1.35 to 9.37)	.010	2.39 (0.78 to 7.34)	.127
Two or more complication v none or only one	5.01 (1.84 to 13.6)	.002	2.93 (0.88 to 9.72)	.079	3.02 (1.20 to 7.60)	.019	1.98 (0.58 to 6.79)	.277
LAR v APR	0.82 (0.37 to 1.79)	.623			0.36 (0.15 to 0.82)	.016	0.51 (0.19 to 1.32)	.163
LAR + ileostomy v APR	1.23 (0.57 to 2.63)	.596			0.91 (0.42 to 1.97)	.802	1.18 (0.48 to 2.92)	.713
Open surgery v minimally invasive	0.98 (0.47 to 2.06)	.967			1.40 (0.68 to 2.88)	.356		

NOTE. Bold indicates statistically significant *P* values for multivariable models to highlight final results.

Abbreviations: ADL, Katz Activities of Daily Living; APR, abdominoperineal resection; ASA, American Society Anesthesiologists; CACI, Charlson Age Comorbidity Index; ECOG PS, Eastern Collaborative Oncology Group performance status; fTRST, Flemish version of the Triage Risk Screening Test; G8, the Geriatric 8; LAR, low anterior resection of the rectum; NRS, Nutritional Risk Screening; OR, odds ratio; QoL, quality of life; TUG, Timed Up & Go.

TABLE 4. Univariable and Multivariable Models for 3- and 6-Month Functional Decline (colon)

Covariates	3-Month Functional Decline (N = 323)				6-Month Functional Decline (N = 325)			
	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P
Age ≥80 v <80 years	1.22 (0.72 to 2.09)	.456	—	—	1.38 (0.81 to 2.35)	.236	—	—
Female v male	1.42 (0.83 to 2.44)	.198			1.38 (0.80 to 2.35)	.247		
ASA SCORE 3-4 v 1-2	1.95 (1.12 to 3.39)	.018	0.86 (0.41 to 1.78)	.677	1.64 (0.95 to 2.83)	.074		
CACI ≥7 v 3-6	3.56 (2.05 to 6.18)	<.001	2.59 (1.26 to 5.32)	.009	2.25 (1.31 to 3.88)	.003	1.03(0.53 to 2.01)	.930
fTRST ≥2 v <2	2.23 (1.29 to 3.84)	.004	1.07 (0.50 to 2.30)	.863	3.14 (1.82 to 5.43)	<.001	2.71 (1.40 to 5.25)	.003
G-8 ≤14 v >14	2.34 (1.10 to 4.97)	.027	1.01 (0.41 to 2.47)	.983	2.05 (0.99 to 4.23)	.053		
PS ECOG ≥2 v 0-1	4.98 (2.63 to 9.41)	<.001	3.12 (1.36 to 7.20)	.007	3.56 (1.86 to 6.80)	<.001	1.51 (0.67 to 3.37)	.319
NRS mildly impaired v normal	1.26 (0.70 to 2.27)	.437			0.85 (0.46 to 1.58)	.615		
NRS moderately + severely impaired v normal	2.03 (0.87 to 4.69)	.098			1.84 (0.80 to 4.24)	.151		
Residential care or living with caregiver v home-independent	1.09 (0.54 to 1.86)	.750			0.67 (0.39 to 1.15)	.153		
Preoperative chemo v no preoperative chemo	0.95 (0.19 to 4.68)	.949			2.19 (0.27 to 17.84)	.463		
Previous delirium v absence	4.61 (1.71 to 12.45)	.003	3.38 (0.95 to 12.00)	.059	2.78 (1.01 to 7.59)	.046	1.11 (0.32 to 3.77)	.871
Open v minimally invasive or robotic	1.88 (1.05 to 3.35)	.031	0.85 (0.38 to 1.91)	.694	2.94 (1.67 to 5.17)	<.001	1.82 (0.93 to 3.55)	.080
Palliative v curative surgery	5.83 (2.24 to 15.14)	<.001	3.31 (0.97 to 11.26)	.056	8.77 (3.15 to 24.35)	<.001	4.11 (1.29 to 13.07)	.017
Complication at surgery								
Only CDI-II v none	1.51 (0.76 to 3.00)	.240	1.05 (0.44 to 2.50)	.915	2.15 (1.13 to 4.08)	.019	1.93 (0.92 to 4.05)	.081
At least CDIII-IV v none	17.33 (7.3 to 40.8)	<.001	12.86 (4.67 to 35.44)	<.001	11.53 (5.01 to 26.54)	<.001	10.32 (3.76 to 28.33)	<.001
Two or more complication v none or only one	3.32 (1.62 to 6.79)	.001	1.36 (0.47 to 3.91)	.567	3.18 (1.56 to 6.47)	.001	0.76 (0.29 to 2.01)	.587

NOTE. Bold indicates statistically significant *P* values for multivariable models to highlight final results.

Abbreviations: ASA, American Society Anesthesiologists; CACI, Charlson Age Comorbidity Index; ECOG PS, Eastern Collaborative Oncology Group performance status; fTRST, Flemish version of the Triage Risk Screening Test; G8, the Geriatric 8; NRS, Nutritional Risk Screening; OR, odds ratio.

TABLE 5. Univariable and Multivariable Models for 3- and 6-Month Functional Decline (rectum)

Covariates	3-Month Functional Decline (N = 133)				6-Month Functional Decline (N = 136)			
	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P	OR for Univariable Model (95% CI)	P	OR for Multivariable Model (95% CI)	P
Age ≥80 v <80 years	2.36 (1.09 to 5.07)	.028	1.84 (0.69 to 4.92)	.224	2.32 (1.08 to 4.98)	.030	1.68 (0.60 to 4.69)	.322
Female v male	1.76 (0.82 to 3.74)	.145			1.43 (0.67 to 3.09)	.359		
ASA SCORE 3-4 v 1-2	3.75 (1.67 to 8.43)	.001	2.36 (0.93 to 6.02)	.072	2.01 (0.93 to 4.37)	.076		
CACI ≥7 v 3-6	3.29 (1.41 to 7.69)	.006	1.70 (0.59 to 4.91)	.326	3.74 (1.66 to 8.41)	.001	2.58 (0.87 to 7.62)	.086
fTRST ≥2 v <2	2.52 (1.14 to 5.58)	.022	0.75 (0.25 to 2.23)	.604	4.24 (1.92 to 9.35)	<.001	1.98 (0.71 to 5.52)	.190
G-8 ≤14 v >14	2.96 (1.19 to 7.42)	.020	1.46 (0.48 to 4.39)	.504	2.57 (1.02 to 6.43)	.044	0.81 (0.26 to 2.58)	.726
ECOG PS ≥2 v 0-1	5.52 (2.05 to 14.82)	.001	2.49 (0.78 to 8.01)	.126	7.91 (3.06 to 20.45)	<.001	4.61 (1.45 to 14.63)	.009
NRS mildly impaired v normal	0.71 (0.29 to 1.79)	.472			1.53 (0.65 to 3.60)	.329		
NRS moderately + severely impaired v normal	0.43 (0.09 to 2.09)	.294			1.84 (0.55 to 6.16)	.321		
Residential care or living with caregiver v home-independent	1.89 (0.84 to 4.23)	.124			1.15 (0.54 to 2.47)	.720		
Preoperative chemo v no preoperative chemo	0.83 (0.38 to 1.79)	.628			0.68 (0.31 to 1.48)	.326		
Previous delirium v absence	13.67 (1.54 to 121.31)	.019	3.68 (0.27 to 50.24)	.328	14.69 (1.65 to 130.41)	.016	3.66 (0.20 to 67.11)	.382
Open v minimally invasive or robotic	1.36 (0.54 to 3.38)	.510			2.02 (0.89 to 4.54)	.091		
Palliative v curative surgery	1.88 (0.40 to 8.79)	.426			4.40 (1.17 to 16.61)	.029	0.75 (0.12 to 4.72)	.760
Complication at surgery								
Only CDI-II v none	3.31 (1.38 to 7.95)	.007	1.92 (0.69 to 5.40)	.214	1.20 (0.48 to 2.93)	.695	0.49 (0.13 to 1.83)	.289
At least CDIII-IV complication v none	4.77 (1.58 to 14.33)	.005	2.34 (0.59 to 9.34)	.229	3.47 (1.23 to 9.71)	.018	1.26 (0.32 to 4.94)	.741
Two or more complication v none or only one	3.33 (1.18 to 9.45)	.023	1.14 (0.31 to 4.21)	.843	3.26 (1.23 to 8.65)	.018	2.26 (0.52 to 9.82)	.278
LAR v APR	0.44 (0.18 to 1.09)	.076			0.50 (0.21 to 1.21)	.123		
LAR + ileostomy v APR	0.45 (0.18 to 1.14)	.094			0.42 (0.16 to 1.10)	.079		

NOTE. Bold indicates statistically significant *P* values for multivariable models to highlight final results.

Abbreviations: ADL, Katz Activities of Daily Living; APR, abdominoperineal resection; ASA, American Society Anesthesiologists; CACI, Charlson Age Comorbidity Index; ECOG PS, Eastern Collaborative Oncology Group performance status; fTRST, Flemish version of the Triage Risk Screening Test; G8, the Geriatric 8; LAR, low anterior resection of the rectum; NRS, Nutritional Risk Screening; OR, odds ratio; TUG, Timed Up & Go.

to maintain their function in most cases (colon cancer 78% and rectal cancer 70%), that older patients can undergo potentially curative (palliative surgery was limited to 5.5% of all cases) major cancer surgery without compromising an important priority: remaining independent.

Important although incomplete outcome measures, such as postoperative morbidity and mortality, stoma rates, and length of stay, have long been the end points driving surgical practice. Such valuable metrics miss important patient priorities such as the impact that major surgery has on their quality of life and FR.

Mortality risk is important to consider and discuss preoperatively, but with rates of postoperative mortality below 3%,⁵ this is an incomplete piece of information to base important decisions on. Producing data on FR, quality of life, and independence is extremely valuable for older patients with cancer to drive shared decision making,^{4,28} while these have been historically extremely difficult to measure in the clinical practice.

The GOSAFE study design invokes a pragmatic proxy, combining the scores of ADL, TUG, and MiniCog. The background for this strategy, supported by the current literature,²⁹⁻³³ is that the milestones for independence are related to performing daily tasks, efficiently ambulating, and having cognitive stability.

The GOSAFE study provides the colorectal cancer multidisciplinary team with the data their patients will be interested to hear about while discussing the effects of surgery in treating life-threatening conditions such as cancer.

Surgeons may look with skepticism at QoL data because of their subjective nature and requirement for patient judgment to define their own satisfaction. Conversely, our results provide the framework to match patients' perspectives with an objective functional measure using three standardized and internationally validated metrics, specifically designed for older patients. There is a statistical correlation between patients who functionally recovered after surgery and those who reported a consistent/improved QoL. However, a number of patients (19.9%–30.8%) who recorded a poor QoL still experienced functional independence according to the ADL, TUG, and MiniCog scores.

The GOSAFE study also shows that the time and resources we spend on the frailty assessment are an investment: several frailty assessment tools explored (ECOG, fTRST, and CACI) and elements of patients' history, commonly neglected in the office discussion (such as the history of delirium), substantially affect postoperative QoL and FR prediction.

In addition, postoperative complications are crucially important in predicting 3-/6-month results. Although specific

complications cannot be accurately anticipated, the institutional/surgeon's rate should be tracked and discussed to warrant full information (including long-term implications on QoL and FR), set expectations, and consider, in selected cases, adapted care.

Because of the crucial role of postoperative complications in affecting QoL and FR, surgeons should ponder the choice of a surgical strategy, as the less stressful surgery could both promote a reduction in mortality and an increase in the chance of maintaining QoL/FR.

MIS (laparoscopic or robotic) correlated with better chances of experiencing FR at 3–6 months in the univariable analysis but missed statistical significance in the multivariable analysis. This is in contrast with some of the current literature showing the positive effects of MIS in older patients.³⁴ The main reason could be found in the long time span from surgery to QoL/FR reassessment (90–120 days), which likely mitigated the positive effect of MIS.

The GOSAFE study also showed that experiencing good QoL and FR is not prevented in patients with a permanent (or temporary) stoma after rectal cancer surgery. The assumption that a restorative procedure conveys a superior QoL and function is not supported by our data. However, our real-world data show how only 67% of patients had their ileostomy reversed during the following months, consistently with the results of other retrospective analyses.^{35,36}

This study has several limitations. First, the PRO measurement tools used for older patients were not designed uniquely for the senior population. However, the EQ-5D-3L has been widely validated in large population studies from Western countries and offers the opportunity to include cognitively impaired patients.²⁵ Second, despite all efforts made to ensure data integrity including the exclusion of centers recruiting <20 consecutive patients, a small proportion of patients were lost to follow-up and a number failed to complete 3-month and 6-month QoL/FR questionnaires (Fig 1). Third, although patients were enrolled prospectively, data were not collected on patients who, for whatever reason, were not considered amenable to surgery on the basis of the single centers' clinical criteria and who underwent a nonoperative pathway on the basis of their cancer stage, frailty, and/or symptoms.

In conclusion, the GOSAFE shows that majority of older patients can experience a restored QoL and FR 3 months after colorectal cancer surgery. Those were much needed but previously unknown data about outcomes that truly matter to patients. Frailty screening tools, history of delirium, and postoperative complications correlate with a worse QoL and FR. These items and their correlation with the restoration of QoL and function should guide the conversation about possible surgical strategies.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Final approval of manuscript: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Predicting Functional Recovery and Quality of Life in Older Patients Undergoing Colorectal Cancer Surgery: Real-World Data From the International GOSAFE Study

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APPENDIX

TABLE A1. Recruiting International Centers

Institution	Department	City	Country	Activation Date
Ospedale "per gli Infermi" AUSL Romagna (Coordinating Center)	U.O. Chirurgia Generale	Faenza (RA)	Italy	February 15, 2017
Ospedale "GB. Morgagni-L. Pierantoni" AUSL Romagna	U.O. Chirurgia Generale e Terapie Oncologiche Avanzate	Forlì (FC)	Italy	February 15, 2017
Ospedale "Ceccarini," AUSL Romagna	U.O. Chirurgia Generale	Riccione (RN)	Italy	May 9, 2017
Ospedale "Guglielmo da Saliceto", AUSL Piacenza	U.O. Chirurgia generale	Piacenza	Italy	July 11, 2017
Humanitas Clinical and Research Center	Division of Colon and Rectal Surgery	Rozzano (MI)	Italy	July 14, 2017
Ospedale "S. Matteo degli Infermi" AUSL Umbria-2	General, Minimally Invasive and Robotic Surgery	Spoletto (PG)	Italy	July 26, 2017
Brigham and Women's Hospital	Thoracic Surgery	Boston (MA)	United States	October 11, 2017
Clinica S. Rita	Department of Colorectal Surgery	Vercelli	Italy	October 18, 2017
IRCCS Istituto Tumori "Giovanni Paolo II"	Department of Surgical Oncology	Bari	Italy	November 22, 2017
University of Pennsylvania, Perelman School of Medicine	Department of Surgery	Philadelphia (PA)	United States	November 22, 2017
University Medical Center Groningen	Department of Surgical Oncology	Groningen	Netherlands	November 30, 2017
ASST Grande Ospedale Metropolitano Niguarda	Chirurgia generale Oncologia e Mininvasiva	Milan	Italy	November 29, 2017
Jagiellonian University Medical College	Department of General, Oncologic and Geriatric Surgery	Krakow	Poland	December 12, 2017
Ospedale Policlinico S. Martino IRCCS	OU General and Oncologic Surgery	Genova	Italy	December 6, 2017
Oslo University Hospital	Department of Surgery	Oslo	Norway	December 12, 2017
ASST Monza - Ospedale di Desio	General and Emergency Surgery	Desio (MB)	Italy	December 18, 2017
Aristotle University of Thessaloniki, Medical School	4th Surgical Department	Thessaloniki	Greece	January 23, 2018
Hospital Universitario y Politécnico La Fe	General and Digestive surgery	Valencia	Spain	February 9, 2018
Roger William Medical Center Providence	Surgical Oncology	Providence (RI)	United States	February 27, 2018
Sapienza University of Rome, Sant'Andrea University Hospital	Emergency Surgery Unit	Rome	Italy	March 27, 2018
Hospital Sao Francisco Xavier	General Surgery	Lisbon	Portugal	April 4, 2018
Rabin Medical Center	Department of Geriatrics	Tel Aviv	Israel	April 26, 2018
Ospedale Policlinico S. Martino IRCCS	Department of Surgical Sciences and Integrated Diagnostics (DISC)	Genova	Italy	May 14, 2018
Hospital General Universitario de Elche, Universidad Miguel Hernández	Colorectal & Gastrointestinal Department	Alicante	Spain	May 21, 2018
Manchester Royal Infirmary, University of Manchester	HPB Unit	Manchester	United Kingdom	July 16, 2018
Cleveland Clinic Foundation	Department of Colorectal Surgery	Weston (FL)	United States	January 11, 2019

TABLE A2. Functional Assessment Indicators

Test	Acronym	Range of Possible Scores	Frailty Indicator Threshold	Purpose
EQ 5D-3L	EQ 5D-3L Index	0-1	Not applicable	Evaluation of QoL assessing patient's mobility, self-care, usual activities, pain, and anxiety, includes a visual scale
EQ 5D-3L	EQ 5D-3L VAS	0-100	Not applicable	
Eastern Collaborative Oncology Group performance status	ECOG PS	0-4	≥1	Evaluation of cancer burden on functional status
Katz Activities of Daily Living	ADL	0-6	<5	Evaluation of functional independence
MiniCog	MiniCog	0-5	≤2	Detection of cognitive impairment in older adults, therefore suitable for a more thorough evaluation
Flemish version of the Triage Risk Screening Test	fTRST	0-6	≥2	Detection of hospitalized geriatric patients at risk for frailty
Timed Up & Go Test	TUG	Not applicable	≥20 seconds	Three-meters walking test to evaluate functional status
Geriatric 8	G8	0-17	≤14	Detection of oncogeriatric patients who may benefit from comprehensive geriatric assessment
Nutritional Risk Screening	NRS	Normal to severely impaired nutritional status	Moderately to severely impaired	Evaluation of nutritional status taking into account BMI, weight loss, and food intake
American Society of Anesthesiology score	ASA	1-5	Not applicable	Evaluation of preoperative general clinical condition and estimation of anesthesiologic risk
Charlson Age Comorbidity Index	CACI	0-42	≥6	Evaluation of cumulative burden of patient's comorbidities

TABLE A3. Correlation Between EQ-5D-3L Index Variation and FR at 3 and 6 Months

3-Month Analysis	FR, No. (%)	FD, No. (%)	Total, No. (%)	<i>P</i> (McNemar test)
Colon				
Better + equal EQ-5D-3L index	194 (76.4)	49 (71.0)	243 (75.2)	.338
Worse EQ-5D-3L index	60 (23.6)	20 (29.0)	80 (24.8)	
Rectum				
Better + equal EQ-5D-3L index	65 (69.2)	19 (48.7)	84 (63.2)	.193
Worse EQ-5D-3L index	29 (30.8)	20 (51.3)	49 (36.8)	
Overall				
Better + equal EQ-5D-3L index	259 (74.4)	68 (63.0)	327 (71.7)	.110
Worse EQ-5D-3L index	89 (25.6)	40 (37.0)	129 (28.3)	
6-Month Analysis	FR, No. (%)	FD, No. (%)	Total, No. (%)	<i>P</i> (McNemar test)
Colon				
Better + equal EQ-5D-3L index	205 (80.1)	16 (41.0)	221 (74.9)	<.001
Worse EQ-5D-3L index	51 (19.9)	23 (59.0)	74 (25.1)	
Rectum				
Better + equal EQ-5D-3L index	72 (73.5)	8 (30.8)	80 (64.5)	.002
Worse EQ-5D-3L index	26 (26.5)	18 (69.2)	44 (35.5)	
Overall				
Better + equal EQ-5D-3L index	277 (78.3)	24 (36.9)	301 (71.8)	<.001
Worse EQ-5D-3L index	77 (21.7)	41 (63.1)	118 (28.2)	

Abbreviations: FD, functional decline; FR, functional recovery.

TABLE A4. SIOG Surgical Task Force/ESSO GOSAFE Study Group

Surname	First Initial	Name	Institute
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(continued on following page)

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Health Questionnaire
English version for the UK
(Validated for Ireland)

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Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

SELF-CARE

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

USUAL ACTIVITIES (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

PAIN / DISCOMFORT

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

ANXIETY / DEPRESSION

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

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☐ We would like to know how good or bad your health is TODAY.
☐ This scale is numbered from 0 to 100.
☐ 100 means the best health you can imagine.
0 means the worst health you can imagine.
☐ Please mark an X on the scale to indicate how your health is TODAY.
☐ Now, write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =

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FIG A1. The EQ-5D-3L questionnaire.

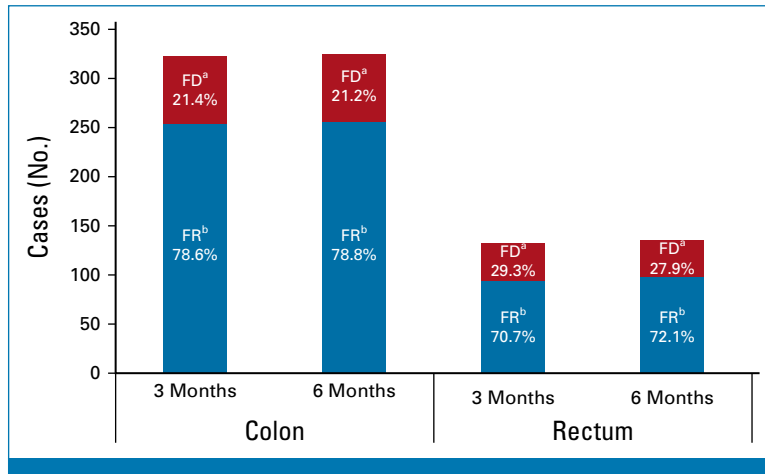


FIG A2. Patients' functional status after major colon and rectal cancer surgery at 3 and 6 months. The only exception was made if a patient was already dependent in one category before surgery and the same one was still deranged at 3 or 6 months; dead patients were included in this category. 3-6 = months after surgery. ^aFD defined for patients who were independent/functional on the combination of ADL, TUG, and MiniCog before surgery but at least 1 of these tests was deranged at 3 or 6 months. ^bPostoperative ADL ≥ 51 + TUG < 20 seconds + MiniCog > 2 or no decline in any domain. FD, functional decline; FR, functional recovery.