Original Article

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Factors associated with functional disability or mortality after elective noncardiac surgery: A prospective cohort study

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Short title: Factors of postoperative functional disability

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Tweetable Summary

Within one year after surgery, one in ten patients experienced postoperative functional disability and one in twenty died. We identified potentially modifiable factors (obesity, poor nutritional status) associated with these adverse outcomes.

Abstract

Purpose:

Preoperative prediction of functional status after surgery is essential when practicing patient-centred medicine. We aimed to evaluate the incidence and factors associated with postoperative functional disability or all-cause mortality. Secondarily, we described the trajectory of disability in this population.

Methods

Adults aged ≥55 years who underwent elective noncardiac surgery under general anesthesia in a tertiary-care hospital were followed up 1 year after surgery. Pre- and intraoperative factors associated with a composite outcome of postoperative functional disability or all-cause mortality were assessed using a multiple logistic regression. The sequential changes in the 12-item WHODAS2.0 score were described overall and stratified by surgical invasiveness.

Results

Of the 2921 patients included, 293 experienced postoperative functional disability (10.0%, 95% CI 8.9-11.1) and 124 died (4.2%, 95% CI 3.5-5.0). In a multiple regression model, potentially modifiable risk factors body mass index ≥30 kg/m^2 and poor preoperative nutritional status were significantly associated with the primary composite outcome, as well as non-modifiable factors such as age, preoperative co-morbidities and blood loss volume. The changes of the 12-item WHODAS2.0 disability score were large variability by surgical invasion and type of surgery such as arthroplasty.

Conclusion

Within one year after surgery, one in ten patients experienced postoperative functional disability and one in twenty died. We identified potentially modifiable factors (obesity, poor nutritional status) associated with these adverse outcomes.

Introduction

Several clinical and observational studies have demonstrated the impact of surgery and anaesthetics on long-term mortality[1,2]. However, relatively few studies have evaluated long-term functional disability after surgery. A previous randomized control trial including 2983 patients and a prospective cohort study with 702 patients revealed a high prevalence of postoperative functional disability (POFD) and mortality 1 year after surgery, with a range of 17.7–18.1%[3,4] Several studies have reported that the patient's physical status -as defined according to the American Society of Anesthesiologists- and the presence of frailty had different effects on the development of POFD[4,5]. However, these studies focused on specific conditions (e.g. frailty).

Preoperative prediction of POFD is essential when practicing patient-centred medicine. Currently, no previous studies have comprehensively investigated factors associated with POFD. Moreover, in addition to preoperative factors, surgical and anesthesia-related factors such as blood loss volume and anaesthetic drugs may influence the incidence of POFD and mortality.

We aimed to evaluate the incidence of POFD and all-cause mortality 1 year after surgery and associated factors. Secondarily, we described the sequential changes in the

12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) score in the overall population and in subpopulations stratified by surgical invasiveness.

Methods

Ethics Approval and Registration (December 31, 2015 University Hospital Medical Information Network, UMIN000021671 (URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000023679)

This prospective observational study was approved by the Nara Medical University Institutional Review Board, Kashihara, Nara, Japan (Chairperson: Prof. M Yoshizumi, Approval No. 1141 on December 25, 2015). All participants provided informed consent.

Inclusion and Exclusion Criteria

Individuals aged ≥55 years who were scheduled for inpatient noncardiac surgery under general anesthesia between April 1, 2016 and December 28, 2018 in our hospital were eligible for inclusion in our study. Patients were excluded if they had previously been enrolled in this study (i.e., reoperation), had diseases requiring psychiatric treatment, or required emergent surgery. Participating patients subsequently completed the WHODAS 2.0 questionnaire, and those who were unable to complete the questionnaire without assistance were excluded. Our hospital is a 992-bed academic medical center with 15 operation rooms, including one hybrid operation room. All patients undergoing elective surgery are evaluated twice in our preoperative assessment clinics. At the first visit when surgery is confirmed, additional investigations such as cardiac ultrasonography are performed as needed, and instructions for medications prior to surgery are provided. The second visit occurs a weekday before surgery, when both patient and medication status are re-evaluated.[6] Research staff recruited patients from the preoperative anesthetic clinic during the patients' second visit.

Data Collection

Before surgery, the patients' age, sex, body mass index (BMI), comorbidities (symptomatic cerebral vascular disease, hypertension, ischemic heart disease, atrial fibrillation, peripheral arterial disease, pacemaker or defibrillator implantation status, asthma, respiratory function, diabetes, and malignant disease), serum albumin and creatinine levels, and nutritional status were assessed. Their nutritional status was assessed using the Mini Nutritional Assessment-short form (MNA-SF), with the total score ranging from 0 to 14 points. The patients' nutritional statuses were defined as follows: normal = 12–14 points, at risk = 8–11 points, and malnourished = 0–7 points[7]. In addition, commonly used drugs (beta blockers, corticosteroids, and statins) were checked because these drugs may have an important impact on postoperative mortality[8,9]. We also collected data regarding anesthetic technique (inhalation agents or propofol), the surgical procedure, duration of surgery, and intraoperative blood loss. Surgical procedures were categorized using a previously reported operative stress score (OSS) as follows: OSS 1, very low stress; OSS 2, low stress; OSS 3, moderate stress; OSS 4, high stress; OSS 5, very high stress[10]. Additionally, any reoperation related to the primary surgery and severe postoperative complications, including cerebral stroke, acute myocardial infarction, prolonged mechanical ventilation, sepsis, pulmonary embolism, and cardiac arrest, were assessed up to 30 days after surgery. Details of the included variables are provided in Supporting Information Table S1.

Primary and Secondary Outcomes

The primary outcome was a composite of the presence of POFD at one year after surgery and all-cause mortality within one year after surgery. A recent consensus guideline for patient-reported outcomes and a systematic review strongly recommend that functional status should be assessed using the 12-item WHODAS 2.0 as a standard clinical endpoint following hospital discharge[11,12]. Functional disability was assessed using the 12-item WHODAS2.0 questionnaire before surgery, at 3 months, and at 1 year after surgery. The 12-item WHODAS 2.0, which is a disability assessment tool, consists of six domains (cognition, mobility, self-care, interacting with other people, life activities, and participation) with a total of 12 items scored. The patient is given five choices per item and the score, depending on the choice, ranges from 1 (no difficulty) to 5 (extreme difficulty). According to the WHO guidelines, the total score ranges from 0% to 100% (where 0 = no disability; 100 = full disability)[13]. At the time of initiating this study, POFD was defined as follows in accordance with previous studies: 1) A 12-item WHODAS2.0 score ≥25% at follow-up for patients with a preoperative 12-item WHODAS2.0 score of <25%, and 2) an increase of 8% if the baseline disability score was ≥25%[14,15]. In 2020, "New onset clinically significant disability" was newly-defined as "increase in WHODAS score of at least 5% to a final WHODAS score of at least 35%"[16] therefore we used this definition for our study analysis. We provided the 12-item WHODAS2.0 questionnaire and a stamped envelope to study patients three months and one year postoperatively. If there was no response, research staff contacted patients or their family by telephone. If there was no response after two telephone calls, the case was classified as no response. Death was ascertained at 3 months and at 1 year after surgery using medical records and responses from bereaved family. Our primary outcome was a composite of POFD and all-cause mortality one year after surgery. Our secondary outcome was the 12-item WHODAS2.0 score.

Statistical Analysis

Continuous data regarding patient demographics are presented as mean (standard deviation (SD)), median (interquartile range (IQR)) and categorical variables as number (%). The incidence of POFD and mortality is presented as a 95% confidential interval (CI), calculated with the Clopper-Pearson exact test. The score of the 12-item WHODAS2.0 are presented as median with 25th to 75th percentiles. The logistic regression models were developed to evaluate factors associated with POFD and death using all variables evaluated in the pre- and intraoperative periods, except for the preoperative 12-item WHODAS2.0 score. The bootstrap procedure repeated 1000 times was employed for internal validation, which estimated the mean odds ratio and mean area under the receiver operating characteristic curve. The 12-item WHODAS2.0 score (median, IQR) was described over the study period overall, as well as stratified by surgical invasiveness (OSS). In a post-hoc analysis, we described the WHODAS2.0

scores over the study period in a subgroup analysis of patients who had undergone joint replacement surgery. All data were analyzed using R (Statistical Environment Package), version 4.0.3. The null hypothesis was rejected if $p < 0.05$ except for the multiple logistic regression for the primary outcome, where a $p < 0.005$ was used to account for comparisons of multiple independent variables of interest.

Sample Size

When this study was planned, little evidence was available regarding the prevalence of POFD and its related factors, however we assumed that the incidence of POFD was approximately 10% based on a prior study[5]. When there were 32 covariates in multiple logistic analysis, based on the minimal criterion of ten events per predictors we would need at least 3200 patients with an event rate of 10% to have 320 cases of POFD and mortality one year after surgery. Considering the dropout rate of 20% by 1 year follow-up, the required minimum number of cases is 4000 in this study.

Missing Data

Regarding preoperative data, we excluded all patients with missing laboratory data from the final analysis. Although the manual for the WHODAS provides guidelines on how to handle missing data, we excluded these patients from the final analysis because almost all patients lacked data on three or more items. In addition, during the follow-up process, we contact subjects twice by phone to minimize missing data.

Results

During this study period, we identified 7117 patients over 55-years of age who were scheduled to undergo elective surgery under general anesthesia. Of the 6,060 patients who met our study criteria, 4402 patients answered the questionnaire without assistance before surgery. Surgery was postponed or cancelled in 226 cases and preoperative data were missing in 156 cases. Of the 4020 patients with complete preoperative data, 3799 patients proceeded with their scheduled surgery. The follow-up rate was 76.8% (2921/3799) and 119 patients provided insufficient data regarding the questions on the 12-item WHODAS2.0 (119/3799) (Figure 1). Multiple imputation was not performed and patients with missing data were excluded from the analysis. Finally, 878 patients were excluded for missing data (759 did not respond and 119 lacked at least one item of the 12-item WHODAS2.0) and 2921 patients (2797 survivors and 124 deceased) were included in the analysis.

Patient characteristics are presented in Table 1. The prevalence of preoperative malnutrition and risk for malnutrition was 4.6% and 31.2%, respectively (Table 1). We explored the characteristics of those who were lost to follow up vs those who were not (Supporting Information Table S2). Several factors including young age, restrictive lung disorders, nutritional disorders, and higher surgical invasiveness score were associated with loss to follow-up.

Reoperation was performed in 2.8% (82/2921) of cases, and severe postoperative complications occurred in 1.7% (52/2921) of the cases (stroke n=15, acute myocardial infarction n=1, prolonged artificial respiration n=27, cardiac arrest n=5, sepsis n=6, pulmonary embolism n=4, some patients have multiple complications.). Thirty day mortality was 0.06% (2/2921).

One year after surgery, 293/2921 (10.0%, 95% CI 8.9-11.1) patients experienced POFD and 124/2921 (4.2%, 95% CI 3.5-5.0) patients died. The incidence of our primary outcome was 14.3% (CI: 13.0-15.6). Of these, there were 390/2921 (13.3%, 95% CI 12.1-14.6) and 20/2921 (0.6%, 95% CI 0.4-1.0) patients with POFD and who died, respectively, at 3 months, with a total incidence of 14.0% (95% CI 12.8-15.3). Age, BMI ≥30 kg.m^{-2}, symptomatic cerebral vascular disease, restrictive lung disease, steroid, serum albumin, nutritional status, and blood loss volume were statistically significant factors associated with POFD at 1 year (Table 3). The mean area under the receiver operating characteristic curve for the model was 0.73 (95% CI 0.70 to 0.75).

The results of changes in the WHODAS2.0 disability score after surgery, stratified by surgical invasiveness are shown in Figure 2 and Supporting Information Table S3. Patients who underwent surgeries with an OSS of 4-5 reported higher rates of disability at the 12-items WHODSA2.0 one year after surgery in contrast with those who underwent surgeries with an OSS of 1-3. (Figure 2 and Supporting Information Table S3 and Figure 1). The sequential changes in the 12-item WHODAS-2.0 score overall and in specific domains are shown in Table 2 and Supporting Information Figure 2, as well as for those who underwent joint arthroplasty (n=156) and we observed similar self-reported disability scores within each domain.

Discussion

Evaluating long-term POFD and mortality is important to achieve health and longevity, especially in an increasingly aging population. One in seven older adults who underwent noncardiac surgery with general anesthesia experienced either POFD or mortality 1 year after surgery. Our data provided some factors related to POFD and mortality, including both potentially modifiable and non-modifiable factors. In this prospective observational study of 2921 patients, we observed that the 12-item WHODAS 2.0 score changed at different time points, and the majority of patients recovered to their preoperative score one year after surgery. These observations require further study about the trajectory of disability after surgery.

In our cohort, 14.3% participants experienced POFD or died 1 year after surgery. Although the prevalence of POFD and death 1 year after surgery varies among studies, given the high prevalence observed in this study and the increasing number of surgeries worldwide, POFD is an issue that needs to be resolved. Our study revealed surgical factors associated with POFD and death included blood loss as well as patient-specific characteristics. Among preoperative patient characteristics, age, and appropriately managed co-morbidities are fixed factors that require careful perioperative management but are difficult to change. In contrast, potentially modifiable factors for a poor outcome included preoperative nutritional status and obesity. Although preoperative malnutrition has been previously associated with postoperative complications, the relationship with longer term POFD is less well understood[17-20]. In this study, we found that preoperative nutritional status was independently associated with POFD and mortality. In recent years, frailty—especially physical frailty—has been focused on potentially modifiable factors, and its association with short-term and long-term outcomes after surgery has been reported[2,4,21,22]. In this study, frailty was not assessed; however, the MNA-SF assessment includes the evaluation of psychological stress and neuropsychological factors, which play a role in the assessment of physical and cognitive frailty [6,23]. Moreover, the benefit of preoperative nutritional support on postoperative outcomes has been widely recognized;however, there are many discrepancies in the duration of intervention and the types of nutrients [24,25]. Future studies are needed to identify strategies to improve preoperative malnutrition, and whether these interventions improve patient-reported outcomes, including POFD, without worsening disease prognosis.

We assessed the sequential score of the 12-item WHODAS2.0; however, the median shown in this study were not able to capture the presence of different trajectories of functional recovery after surgery - with some cases being associated with improved function and others with decreased function. In fact, there were different postoperative courses between patients underwent joint surgery and entire patients. In the future, a large study is needed to understand functional disability after specific surgeries.

In our cohort, the incidence of complications and mortality after surgery were relatively low. This may have resulted from several factors: i) we evaluated only serious postoperative complications, such as diseases requiring intensive care or reoperation classified as IIIb or IV according to the Clavien–Dindo classification[26], ii) 76.5% of the surgeries were of lower invasiveness (OSS 1–3), and iii) all patients undergoing elective surgery were evaluated twice in our preoperative assessment clinics. The impact of our institution's unique preoperative system on the low complication rate has not been investigated and the exact reason has been unclear; however, it may be explained by the change of surgical procedures to minor ones and the preoperative patients' optimization based on information provided in our preoperative assessment clinics.

Our study has several limitations. First, this study included only patients who underwent surgery and were able to fill in the questionnaire by themselves. Furthermore, patients who lacked complete data were excluded from the analysis. Our results need to be interpreted with caution because we were more likely to exclude patients who were more vulnerable or cognitively impaired and who may be more likely to die or develop a new disability after surgery. Moreover, as a post hoc analysis, background of patients who lost contact during 1 year is shown in Supporting Information Table S2, which includes factors such as younger age, restrictive lung disorders, poor nutritional status, and higher surgical invasiveness. The exact reason why younger age was a significant factor has been unclear; however, the incidence of 14.3% may be underestimated because some covariates were also associated with POFD. These facts explain that missing data may not have occurred at random and may have introduced bias. Second, we only examined the predictive performance our model and the external validity was not assessed. Third, postoperative functional status is affected by factors other than those evaluated in this study. Finally, the generalisability of our findings may be limited due to the nature of a single-centre study.

In conclusion, in a large-scale prospective observational study, we found that one in seven patients aged ≥55 years who underwent elective noncardiac surgery with general anesthesia experienced POFD or mortality 1 year postoperatively, and potentially modifiable factors, including nutritional status and obesity, were related to these adverse outcomes. As the number of surgeries increases in an aging population, preoperative risk assessment and provision of postoperative outcomes should be included in shared surgical decision-making and informed consent to achieve health and longevity. Future intervention trials are needed to evaluate whether preoperative patient optimization, including nutritional intervention, can improve long-term functional status.

Trial Registration: University Hospital Medical Information Network, UMIN000021671 (URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000023679).

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Role of the funding source

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Competing Interests: The authors declare no competing interests.

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Tables

Table 1 Demographics of patients who underwent noncardiac surgery with general anesthesia with and without postoperative functional disability or mortality. The values are represented as mean (SD) or number (%).

Characteristic	Total	Presence of postoperative functional disability or mortality (+)	Absence of postoperative functional disability or mortality (-)	Mean difference (95% confidence interval)	P value
	N = 2921	*N* = 417	*N* = 2504		
Age(yr) , mean (SD)	69.6 (7.5)	72.6 (7.4)	69.1(7.4) (7.4)	3.4 (2.7 to 4.2)	<0.001

Male, n/total *N* (%)	1631(55.8%)	249(59.7%)	1122(44.8%)		0.09
Body mass index(kg/m^2), mean(SD)	23.3 (3.6)	23.2(3.8)	23.4 (3.5)	-1.9 (-5.7 to 0.1)	0.3
categorical data					0.002
< 18.5, n/total N (%)	189(6.4%)	39(9.3%)	150(5.9%)		
18.5≦, <25, n/total N (%)	1879(64.3%)	264(63.3%)	1615(64.5%)		
25≦, < 30, n/total N (%)	738(25.2%)	89(21.3%)	649(25.9%)		
30≦, n/total N (%)	115(3.9%)	25(6.0%)	90(3.6%)		
Comorbidity					
Symptomatic cerebral vascular disease, n/total N (%)	273(9.3%)	65(15/5%)	208(8.3%)		<0.001
Hypertension, n/total N (%)	1566(53.6%)	248(59.5%)	1318(52.6%)		0.01

Ischemic heart disease, n/total N (%)	208(7.1%)	45(10.8%)	163(6.5%)	0.002
Atrial fibrillation, n/total N (%)	84(2.8%)	17(4.1%)	67(2.7%)	0.15
Peripheral arterial disease, n/total N (%)	35(1.2%)	7(1.7%)	28(1.1%)	0.46
Pacemaker or defibrillator, n/total N (%)	15(0.5%)	5(1.2%)	10(0.4%)	0.08
Asthma, n/total N (%)	127(4.3%)	17(4.1%)	110(4.4%)	0.87
Diabetes, n/total N (%)	548(18.7%)	109(26.1%)	439(17.5%)	<0.001
Malignant disease, n/total N (%)	1834(47.3%)	229(54.9%)	1154(46.0%)	<0.001
Respiratory function				<0.001
Normal, n/total N (%)	2107(72.1%)	258(61.8%)	1814(72.4%)	
Obstructive lung disease, n/total N (%)	675(23.1%)	109(26.1%)	566(22.6%)	
Restrictive lung disease, n/total N (%)	174(0.59%)	50(12.0%)	124(5.0%)	

Medication					
β-blocker, n/total N (%)	186(6.3%)	37(8.9%)	149(6.0)		0.03
Steroid, n/total N (%)	94(3.2%)	30(7.2%)	64(2.6%)		<0.001
Statin, n/total N (%)	536(18.3%)	75(18.0)	461(18.4%)		0.88
Laboratory data					
Serum albumin (g/dL) , mean (SD)	4.2(0.3)	4.0(0.4)	4.2(0.3)	-0.1(-0.2 to -0.1)	<0.001
Serum creatinine (mg/dL) , mean (SD)	0.92(0.92)	1.11(1.20)	0.90(0.86)	0.2(0.1 to 0.3)	<0.001
Nutritional status					<0.001
Normal , n/total N (%)	1873(66.9%)	213(51.0%)	1660(66.2%)		
At risk of malnutrition , n/total N (%)	912(31.2%)	166(39.8%)	746(29.8%)		
Malnutrition, n/total N (%)	136(4.6%)	38(9.1%)	98(3.9%)		

Preoperative the 12-items WHODAS2.0				10.9(9.1 to 12.6)	
score , mean (SD)	14.5(17.5)	23.9(18.8)	13.0(16.8)		<0.001
Anesthetic drug					<0.001
Propofol, n/total N (%)	827(28.3%)	89(21.3%)	738(29.4%)		
Inhalation agents, n/total N (%)	2094(71.6%)	328((78.6%)	1766(70.4%)		
Duration of surgery(min), mean (SD)	203(142)	224 (167)	199(137)	25(10 to 39)	0.001
Blood loss volume(mL), mean (SD)	146(480)	235 (816)	133 (397)	101(51 to 150)	<0.001
categorical data					<0.001
0≦, < 99, n/total N (%)	2080(71.2%)	252(60.4%)	1828(73.0%)		
100≦, < 499, n/total N (%)	629(21.5%)	120(28.8%)	509(20.3%)		
500≦, n/total N (%)	212(7.2%)	45(10.8%)	167(6.7%)		

Operative stress score					0.003
	1, n/total N (%)	204(6.9%)	27(6.5%)	177(7.1%)	
	2, n/total N (%)	822(28.1%)	98(23.5%)	724(28.9)	
	3, n/total N (%)	1214(41.5%)	168(40.3%)	1046(41.8%)	
	4, n/total N (%)	530(18.1%)	90(21.6)	440(17.6%)	
	5, n/total N (%)	151(5.1%)	34(8.2%)	117(4.7%)	

WHODAS 2.0 = World Health Organization Disability Assessment Schedule 2.0; SD = standard deviation

Table 2. Sequential changes in the 12-item World Health Organization Disability Assessment Schedule 2.0 score on the specific domains in total patients and patients who had arthroplasty (knee and hip)

Total patients (N = 2797)

		Preoperative	3 month	12 month
		Median [Q1, Q3]	Median [Q1, Q3]	Median [Q1, Q3]
Cognitive	Learning	0 [0, 1]	0 [0, 1]	0 [0, 1]
	Concentration	0 [0, 0]	0 [0, 0]	0 [0, 0]
Mobility	Standing	0 [0, 1]	0 [0, 1]	0 [0, 1]
	Walking	0 [0, 1]	1 [0, 1]	0 [0, 1]
Self-care	Washing	0 [0, 0]	0 [0, 0]	0 [0, 0]

	Dressing	0 [0, 0]	0 [0, 0]	0 [0, 0]
Getting along	Dealing with people	0 [0, 0]	0 [0, 0]	0 [0, 0]
	Maintaining friendship	0 [0, 0]	0 [0, 0]	0 [0, 0]
Life activities	Day to day work	0 [0, 0]	0 [0, 0]	0 [0, 1]
	Household responsibilities	0 [0, 1]	0 [0, 1]	0 [0, 1]
Participation	Community activities	0 [0, 1]	0 [0, 1]	0 [0, 1]
	Emotional impact	1 [0, 2]	1 [0, 1]	1 [0, 1]
	Total(%)	8.3 [2.7, 19.4]	11.1 [2.7, 25.0]	8.3 [0.0, 25.0]

Q1, first quartile; Q3, third quartile

Each item has the score 0 to 4. Total score is changed to percentage using following formula, (sum score / 48)*100.

Arthroplasty (knee and hip) (N = 156)

		Preoperative Median [Q1, Q3]	3 month Median [Q1, Q3]	12 month Median [Q1, Q3]
Cognitive	Learning	1 [0, 2]	1 [0, 2]	0 [0, 1]
	Concentration	0 [0, 0.2]	0 [0, 1]	1 [0, 1]
Mobility	Standing	2 [1, 3]	1 [0, 2]	1 [0, 2]
	Walking	3 [1, 3]	1 [1, 2]	1 [0, 2]
Self-care	Washing	0 [0, 1]	0.5 [0, 1]	0 [0, 1]
	Dressing	1 [0, 1]	0 [0, 1]	0 [0, 1]
Getting along	Dealing with people	0 [0, 0]	0 [0, 0]	0 [0, 0]

	Maintaining friendship	1 [0, 0]	0 [0, 1]	0 [0, 0]
Life activities	Day to day work	1 [0, 1]	1 [0, 1]	0 [0, 1]
	Household responsibilities	1 [1, 1]	1 [1, 1]	1 [0, 1]
Participation	Community activities	1 [0, 2]	1[1, 1]	1 [0, 1]
	Emotional impact	1 [0, 2]	1 [0, 2]	1 [0, 1]
	Total(%)	29.1 [19.4, 44.4]	22.2 [13.8, 36.1]	19.4 [8.3, 33.3]

Q1, first quartile; Q3, third quartile

Each item has the score 0 to 4. Total score is changed to percentage using following formula, (sum score / 48)*100.

Table 3 Multiple logistic regression analysis for predicting patients with postoperative functional disability or mortality at 1 year after surgery

		Odds ratio (99.5% Confidence interval)	p value
Age(yr)		1.06 (1.03 to 1.08)	<0.001
Female		1.06 (0.68 to 1.55)	0.63
Body mass index(kg/m^2)			
	< 18.5	1.00 (0.51 to 1.83)	0.99
	18.5≦, <25	1	
	25≦, <30	0.92 (0.60 to 1.41)	0.52

30≦	2.56 (1.05 to 5.19)	0.001
Comorbidity		
Symptomatic cerebral vascular disease	1.94 (1.02 to 3.22)	<0.001
Hypertension	0.95 (0.70 to 1.41)	0.71
Ischemic heart disease	1.37 (0.72 to 2.39)	0.14
Atrial fibrillation	1.07 (0.43 to 2.46)	0.79
Peripheral arterial disease	0.76 (0.06 to 2.77)	0.57
Pacemaker or defibrillator	2.27 (0.00 to 20.7)	0.17
Asthma	0.80 (0.30 to 2.03)	0.43
Diabetes	1.36 (0.91 to 2.10)	0.02
Malignant disease	1.27 (0.92 to 1.74)	0.04

Respiratory function			
	Normal	1	
	Obstructive lung disease	1.07 (0.72 to 1.55)	0.65
	Restrictive lung disease	1.80 (1.03 to 3.07)	0.003
Medication			
	β-blocker	0.98 (0.50 to 1.78)	0.95
	Steroid	2.77 (1.21 to 5.28)	<0.001
	Statin	0.85 (0.50 to 1.26)	0.27
Laboratory data			
	Serum albumin (g/dL)	0.55 (0.35 to 0.85)	<0.001
	Serum creatinine (mg/dL)	1.14 (0.97 to 1.33)	0.008

Nutritional status			
	Normal	1	
	At risk of malnutrition	1.55 (1.06 to 2.15)	0.001
	Malnutrition	2.30 (1.09 to 4.73)	0.002
Anesthetic drug			
	Propofol	1	
	Inhalation agents	1.20 (0.79 to 1.91)	0.21
Duration of surgery(min)		1.00 (0.99 to 1.00)	0.62
Blood loss volume(mL)			
	0≦, ＜99	1	
	100≦, ＜499	1.56 (1.01 to 2.36)	0.001

	500≦	1.67 (0.84 to 3.30)	0.02
Operative stress score			
	1	1	
	2	1.07 (0.50 to 2.53)	0.80
	3	0.98 (0.45 to 2.38)	0.95
	4	1.12 (0.55 to 2.72)	0.69
	5	1.14 (0.97 to 1.33)	0.71

NA, Not available

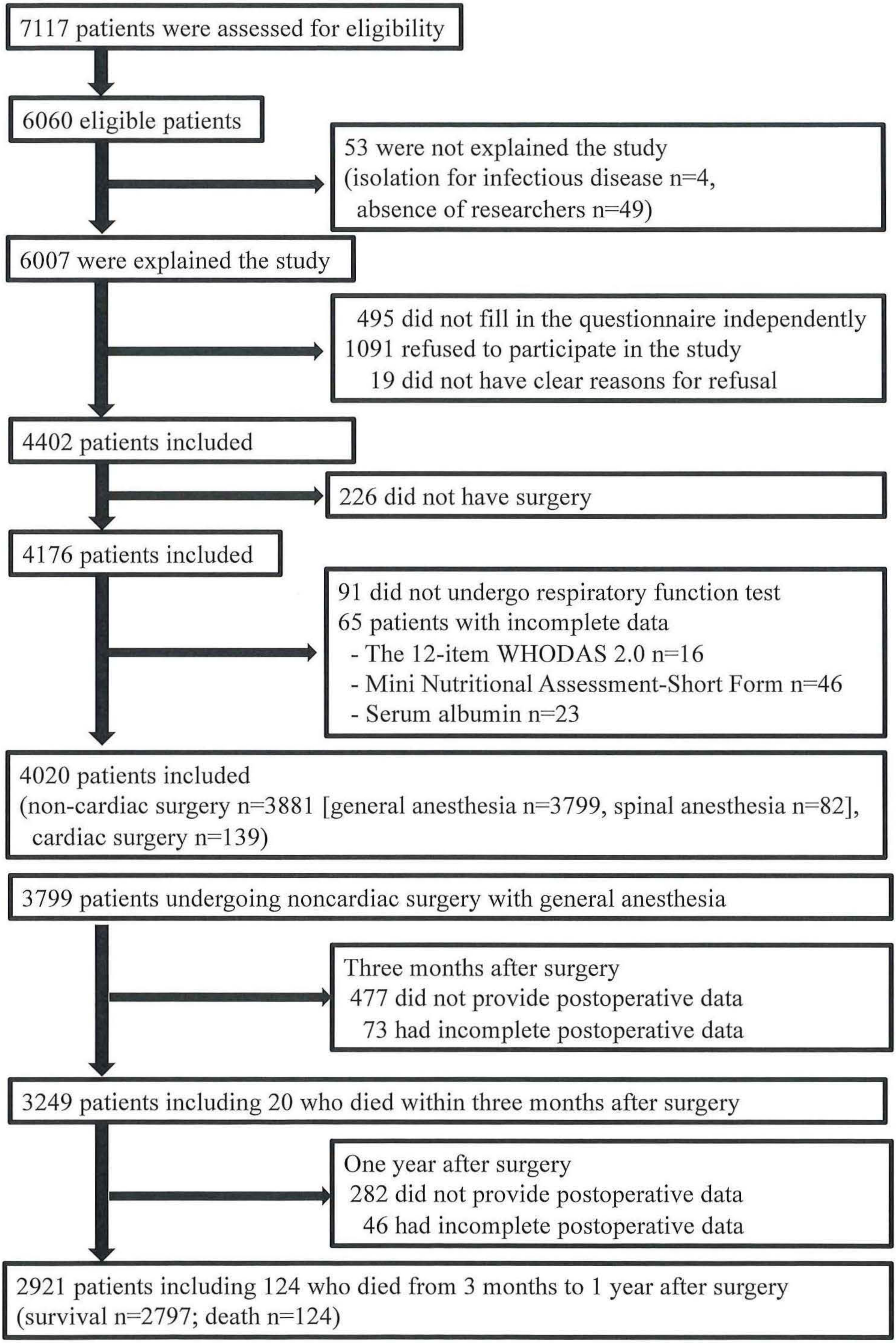
Figure Legends

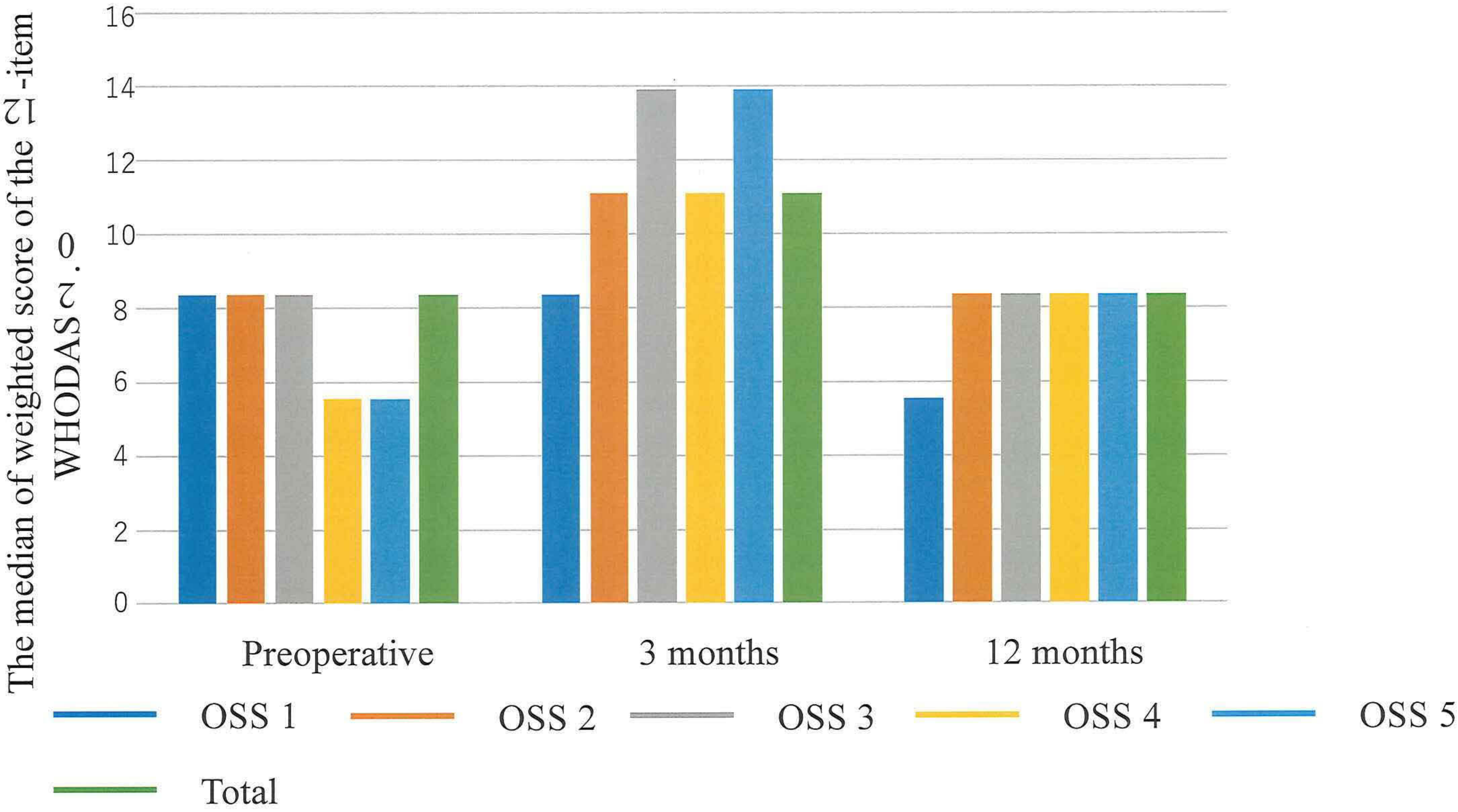
Figure 1 Flowchart of patient selection for noncardiac surgery with general anesthesia.

Figure 2 The sequential changes in the 12-item WHODAS2.0 score according to the Operative Stress Score in patients who underwent noncardiac surgery with general anesthesia.

WHODAS, World Health Organization Disability Assessment Schedule.

The 12-item WHODAS2.0 score in patient underwent surgeries with OSS2 and in overall patients followed the same trajectory; therefore, the graph shows the overall trend.


7117 patients were assessed for eligibility
6060 eligible patients
53 were not explained the study
(isolation for infectious disease n=4,
absence of researchers n=49)
6007 were explained the study
495 did not fill in the questionnaire independently
1091 refused to participate in the study
19 did not have clear reasons for refusal
4402 patients included
226 did not have surgery
4176 patients included
91 did not undergo respiratory function test
65 patients with incomplete data
- The 12-item WHODAS 2.0 n=16
- Mini Nutritional Assessment-Short Form n=46
- Serum albumin n=23
4020 patients included
(non-cardiac surgery n=3881 [general anesthesia n=3799, spinal anesthesia n=82],
cardiac surgery n=139)
3799 patients undergoing noncardiac surgery with general anesthesia
Three months after surgery
477 did not provide postoperative data
73 had incomplete postoperative data
3249 patients including 20 who died within three months after surgery
One year after surgery
282 did not provide postoperative data
46 had incomplete postoperative data
2921 patients including 124 who died from 3 months to 1 year after surgery
(survival n=2797; death n=124)



The median of weighted score of the 12-item WHODAS 2.0
16
14
12
10
8
6
4
2
0
Preoperative
3 months
12 months
OSS 1
OSS 2
OSS 3
OSS 4
OSS 5
Total

Supporting Information Table S1 Definitions of patients' comorbidities and commonly used drugs

Symptomatic cerebral vascular disease	Patients with symptomatic stroke and symptomatic carotid artery stenosis
Hypertension	Patients taking medication
Ischemic heart disease	Patients with a history of or scheduled CABG or PCI
Atrial fibrillation	Patients diagnosed chronic atrial fibrillation as per electrocardiogram findings
Peripheral arterial disease	Patients diagnosed or scheduled for surgery
Asthma	Patients taking medications
Respiratory function	
Obstructive respiratory dysfunction	Patients with < 70% forced expiratory volume 1.0 (s) %
Restrictive respiratory dysfunction	Patients with < 80% vital capacity
Dialysis	Patients on hemodialysis or peritoneal dialysis
Diabetes	Patients taking oral diabetes drugs or injecting insulin
Pacemaker or defibrillator	Patients with an implantable pacemaker or defibrillator
Commonly used drugs	
β-Blocker	Patients receiving oral or intravenous beta blockers
Corticosteroid	Patients receiving oral or intravenous corticosteroids
Statin	Patients receiving statins

CABG coronary artery bypass graft, PCI percutaneous coronary intervention

Supporting Information Table S2 Associated factors with patients who had no contact by 1 year after surgery using multiple logistic analysis

	Odds ratio (95% Confidence interval)	p value
Age(yr)	0.98 (0.97 to 0.99)	0.02
Female	1.04 (0.87 to 1.23)	0.64
Body mass index(kg/m^2)		
< 18.5	0.71 (0.50 to 1.00)	0.05
18.5≦, <25	1	
25≦, <30	0.98 (0.81 to 1.19)	0.88
30≦	1.57 (1.11 to 2.22)	0.01
Comorbidity		
Symptomatic cerebral vascular disease	1.26 (0.98 to 1.61)	0.06
Hypertension	0.95 (0.81 to 1.13)	0.61
Ischemic heart disease	1.20 (0.88 to 1.62)	0.23
Atrial fibrillation	1.21 (0.78 to 1.88)	0.37
Peripheral arterial disease	1.18 (0.59 to 2.33)	0.63
Pacemaker or defibrillator	1.53 (0.65 to 3.63)	0.32
Asthma	0.89 (0.60 to 1.31)	0.56

Diabetes	0.90 (0.73 to 1.10)	0.32
Malignant disease	1.03 (0.87 to 1.22)	0.71
Respiratory function		
Normal	1	
Obstructive lung disease	1.05 (0.87 to 1.28)	0.55
Restrictive lung disease	1.53 (1.15 to 2.03)	0.003
Medication		
β-blocker	0.94 (0.67 to 1.30)	0.71
Steroid	0.70 (0.44 to 1.12)	0.14
Statin	0.98 (0.80 to 1.22)	0.91
Laboratory data		
Serum albumin (g/dL)	0.68 (0.55 to 0.85)	0.001
Serum creatinine (mg/dL)	1.01 (0.93 to 1.09)	0.79
Nutritional status		
Normal	1	
At risk of malnutrition	1.52 (1.06 to 2.18)	0.02
Malnutrition	1.21 (1.00 to1.45)	0.04
Preoperative WHODAS2.0 weighted score	1.01 (1.00 to 1.01)	<0.001
Anesthetic drug		
Propofol	1	
Inhalation agents	1.04 (0.86 to 1.25)	0.68

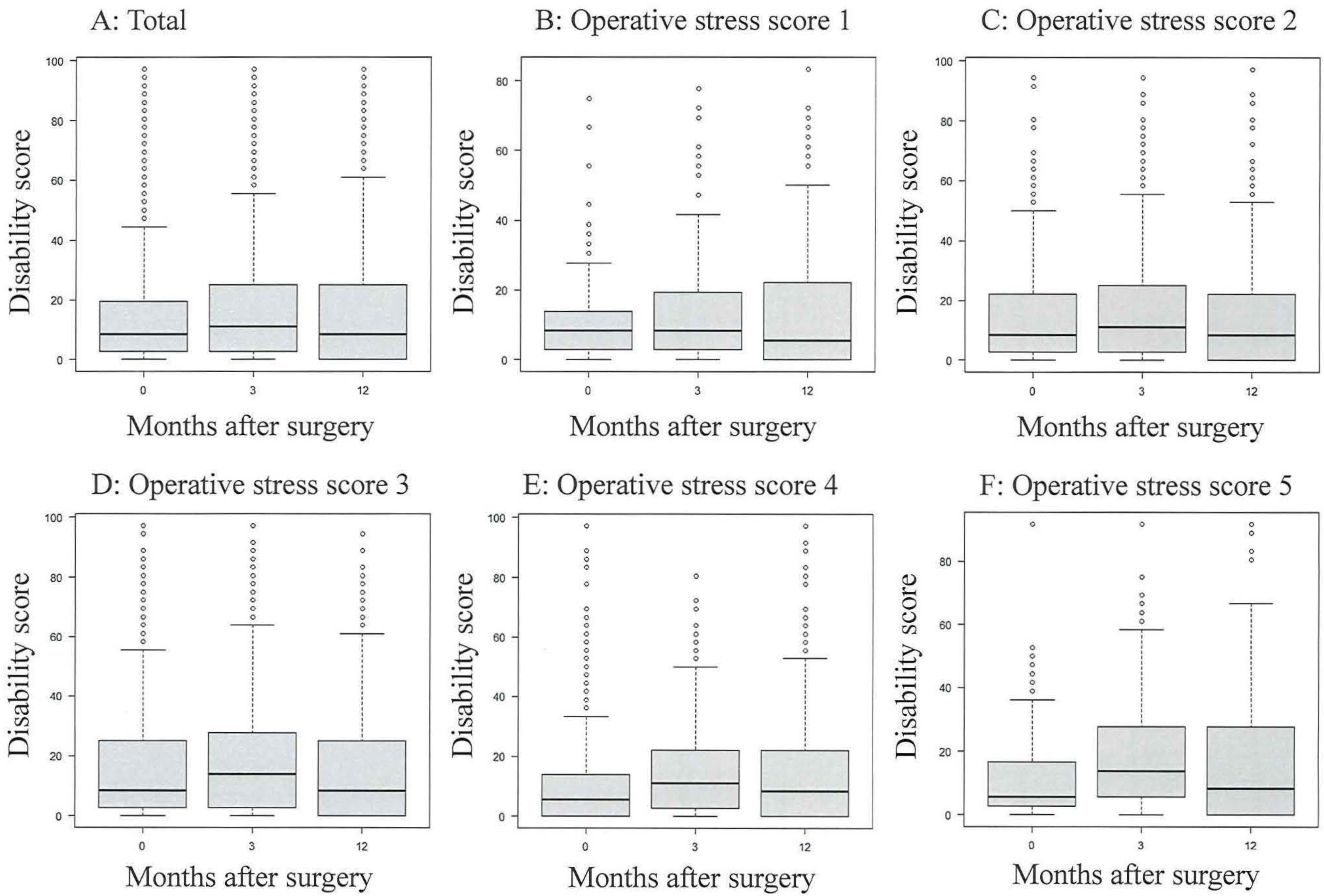
Duration of surgery(min)		1.00 (0.99 to 1.00)	0.72
Blood loss volume(mL)			
	0≦, ＜99	1	
	100≦, ＜499	0.95 (0.77 to 1.19)	0.7
	500≦	0.93 (0.65 to 1.33)	0.69
Operative stress score			
	1	1	
	2	0.70 (0.52 to 0.95)	0.02
	3	0.60 (0.44 to 0.82)	0.002
	4	0.75 (0.53 to 1.04)	0.09
	5	0.49 (0.30 to 0.80)	0.005

WHODAS 2.0; World Health Organization Disability Assessment Schedule 2.0

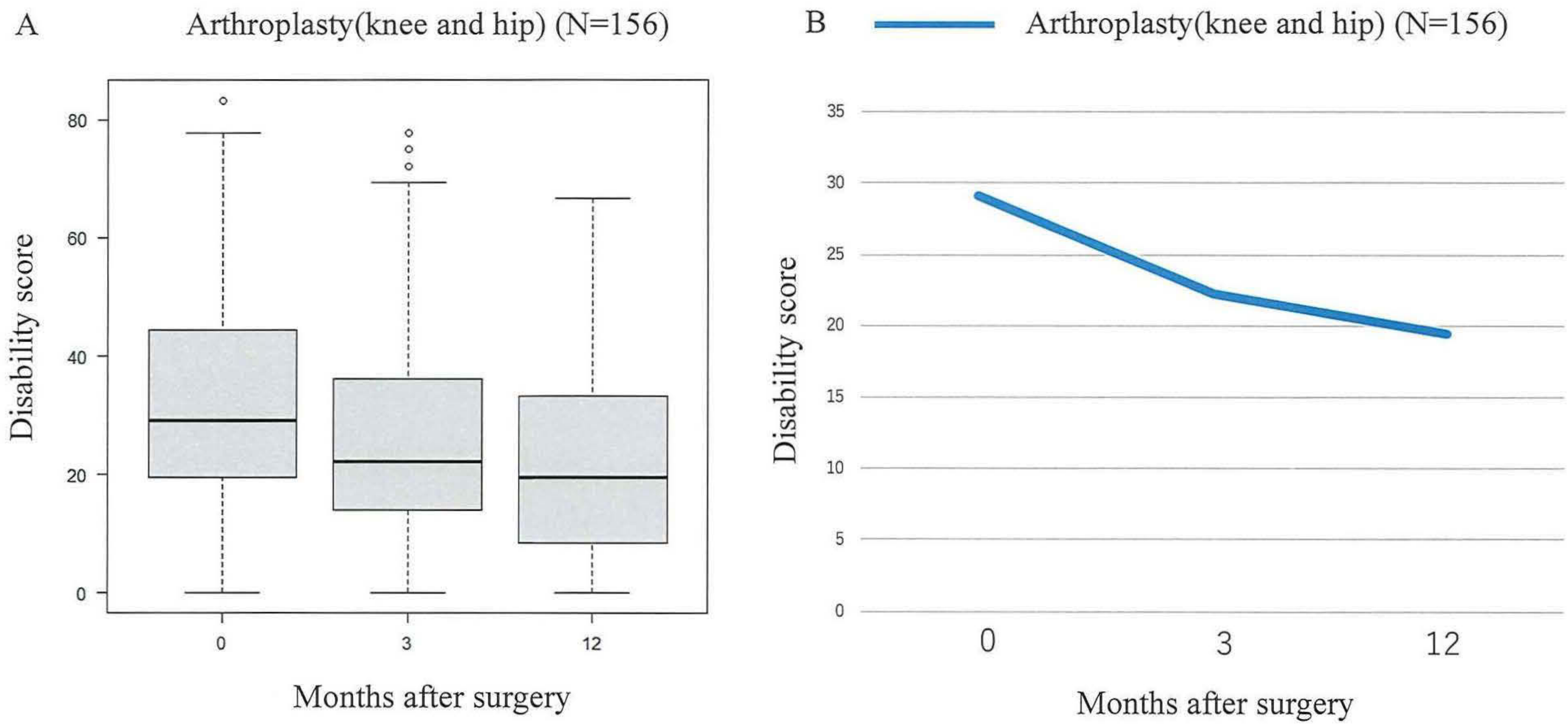
Supporting Information Table S3 Sequential changes in the 12-item WHODAS 2.0 score by the operative stress score

Operative stress score	Preoperative Median [Q1, Q3]	3 months later Median [Q1, Q3]	12 months later Median [Q1, Q3]
1 (n = 204)	8.33 [2.77, 13.8]	8.33 [2.77, 19.4]	5.55 [0.0, 22.2]
2 (n = 822)	8.33 [2.77, 22.2]	11.1 [2.77, 25.0]	8.33 [0.0, 22.2]
3 (n = 1214)	8.33 [2.77, 25.0]	13.8 [2.77, 27.7]	8.33 [0.0, 25.0]
4 (n = 530)	5.55 [0.0, 14.5]	11.1 [2.77, 22.2]	8.33 [0.0, 25.0]
5 (n = 151)	5.55 [2.77, 16.6]	13.8 [5.55, 27.7]	8.33 [0.0, 27.7]
Total (n = 2921)	8.33 [2.77, 19.4]	11.1 [2.77, 25.0]	8.33 [0.0, 25.0]

WHODAS 2.0, World Health Organization Disability Assessment Schedule 2.0; Q1, first quartile; Q3, third quartile



A: Total
B: Operative stress score 1
C: Operative stress score 2
D: Operative stress score 3
E: Operative stress score 4
F: Operative stress score 5
Disability score
Months after surgery
0
3
12
0
20
40
60
80
100


A
Arthroplasty(knee and hip) (N=156)
Disability score
0
20
40
60
80
0
3
12
Months after surgery
B
Arthroplasty(knee and hip) (N=156)
Disability score
0
5
10
15
20
25
30
35
0
3
12
Months after surgery