Can J Anesth/J Can Anesth (2022) 69:704–714
https://doi.org/10.1007/s12630-022-02247-8

REPORTS OF ORIGINAL INVESTIGATIONS

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

# Facteurs associés à l'incapacité fonctionnelle ou à la mortalité après une chirurgie non cardiaque non urgente : une étude de cohorte prospective

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Received: 1 June 2021 / Revised: 19 December 2021 / Accepted: 22 December 2021 / Published online: 8 April 2022


**Abstract**

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

**Methods** *Adults aged ≥ 55 yr who underwent elective noncardiac surgery under general anesthesia in a tertiary care hospital were followed up one 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 World Health Organization Disability Assessment Schedule (WHODAS) 2.0 score were described and stratified by surgical invasiveness.*

**Results** *Of the 2,921 patients included, 293 experienced postoperative functional disability (10.0%; 95% confidence interval [CI], 8.9 to 11.1) and 124 died (4.2%; 95% CI, 3.5 to 5.0). In a multiple regression model, the 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 nonmodifiable factors such as age, preoperative comorbidities, and blood loss volume. Changes in the 12-item WHODAS 2.0 disability score varied between different levels of surgical invasiveness and types of surgery.*

**Conclusion** *Within one year after surgery, one in ten patients experienced postoperative functional disability and one in 20 died. We identified potentially modifiable factors (obesity, poor nutritional status) associated with these adverse outcomes.*

**Study registration** *University Hospital Medical Information Network (UMIN000021671); registered 31 December 2015.*

**Résumé**

**Objectif** *La prédiction préopératoire du statut fonctionnel après chirurgie est essentielle dans la pratique d'une médecine centrée sur le patient. Nous avons cherché à évaluer l'incidence et les facteurs associés à l'incapacité fonctionnelle ou à la mortalité toutes causes confondues en postopératoire. En deuxième lieu, nous avons cherché à décrire la trajectoire de l'incapacité dans cette population.*

**Méthode** *Les adultes âgés de ≥ 55 ans qui ont subi une chirurgie non cardiaque non urgente sous anesthésie générale dans un hôpital de soins tertiaires ont été suivis jusqu'à un an après leur chirurgie. Les facteurs pré- et peropératoires associés à un devenir composite d'incapacité fonctionnelle postopératoire ou de mortalité toutes causes confondues ont été évalués à l'aide d'une régression logistique multiple. Les changements séquentiels dans le score de l'outil d'évaluation de*

This article is accompanied by an editorial. Please see Can J Anesth 2022; this issue.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s12630-022-02247-8.

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*l'invalidité de l'Organisation mondiale de la Santé (WHODAS - World Health Organization Disability Assessment Schedule) version 2.0 en 12 éléments ont été décrits et stratifiés en fonction du degré invasif de la chirurgie.*

**Résultats** *Sur les 2921 patients inclus, 293 ont présenté une incapacité fonctionnelle postopératoire (10,0 %; intervalle de confiance [IC] à 95 %, 8,9 à 11,1) et 124 personnes sont décédées (4,2 %; IC 95 %, 3,5 à 5,0). Dans un modèle de régression multiple, les facteurs de risque potentiellement modifiables, un indice de masse corporelle ≥ 30 kg·m$^{-2}$ et un mauvais état nutritionnel préopératoire étaient significativement associés au critère d'évaluation composite principal, ainsi qu'à des facteurs non modifiables tels que l'âge, les comorbidités préopératoires et le volume de perte de sang. Les changements dans le score d'incapacité WHODAS 2.0 à 12 éléments variaient entre les différents degrés invasifs de la chirurgie et les types de chirurgie.*

**Conclusion** *Dans l'année qui a suivi la chirurgie, un patient sur dix a présenté une incapacité fonctionnelle postopératoire et un sur 20 est décédé. Nous avons identifié des facteurs potentiellement modifiables (obésité, mauvais état nutritionnel) associés à ces effets indésirables.*

**Enregistrement de l'étude** *University Hospital Medical Information Network (UMIN000021671); enregistré le 31 décembre 2015.*

**Keywords** nutrition assessment · patient-reported outcome measures · patient safety · perioperative medicine · perioperative period

Several clinical and observational studies have shown the impact of surgery and anesthetics on long-term mortality.[1,2] Nevertheless, relatively few studies have evaluated long-term functional disability after surgery. A previous randomized controlled trial including 2,983 patients and a prospective cohort study with 702 patients revealed a high prevalence of postoperative functional disability (POFD) and mortality one year after surgery, with a range of 17.7–18.1%.[3,4] Several studies have reported that the patients' American Society of Anesthesiologists Physical Status and the presence of frailty had different effects on the development of POFD.[4,5] Nevertheless, these studies focused on specific conditions (e.g., frailty).

Preoperative prediction of POFD is essential when practicing patient-centered medicine. Currently, no studies have comprehensively investigated factors associated with POFD. In addition to preoperative factors, surgical and anesthesia-related factors such as blood loss volume and anesthetic drugs may influence the incidence of POFD and mortality but these relationships are not well defined. We aimed to evaluate the incidence and factors associated with POFD and all-cause mortality one year after surgery. We also sought to describe 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

This prospective observational study was registered on the University Hospital Medical Information Network (31 December 2015; UMIN000021671; URL: https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr_view.cgi?recptno=R000023679). This study was approved by the Nara Medical University Institutional Review Board (Kashihara, Nara, Japan; Chairperson, Prof. M Yoshizumi; approval number 1141; 25 December 2015). All participants provided informed consent.

### Inclusion and exclusion criteria

Individuals aged ≥ 55 yr who were scheduled for inpatient noncardiac surgery under general anesthesia between 1 April 2016 and 28 December 2018 in our hospital (Nara Medical University Hospital, Kashihara, Nara, Japan) 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. Participants were then asked to complete the WHODAS 2.0 questionnaire, and those who were unable to complete the questionnaire without assistance were excluded. Our hospital is a 992-bed tertiary care academic medical center with 15 operating rooms, including one hybrid operating 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, and 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 status was 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 they can have an important impact on postoperative mortality.[8,9] We also collected data on 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, and 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 the Electronic Supplementary Material (ESM) (eTable 1).

## Primary and secondary outcomes

The primary outcome was a composite of POFD and all-cause mortality one year after surgery. A recent consensus guideline for patient-reported outcomes and a systematic review strongly recommended 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 WHODAS 2.0 questionnaire before surgery, at three months, and at one 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 WHO guidelines, the total score ranges from 0% to 100% (where 0% indicates no disability and 100% indicates full disability).[13] At the time of initiating this study, POFD was defined as follows in accordance with the previous studies: 1) a 12-item WHODAS 2.0 score $\geq$ 25% at follow-up for patients with a preoperative 12-item WHODAS 2.0 score of < 25%, and 2) an increase of 8% if the baseline disability score was $\geq$ 25%.[14,15] In 2020, "new onset clinically significant disability" was newly defined as "an increase in WHODAS score of at least 5% to a final WHODAS score of at least 35%,"[16] so we used this definition for our study analysis. We provided the 12-item WHODAS 2.0 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 three months and at one 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 WHODAS 2.0 score.

## Statistical analysis

Continuous data regarding patient demographics are presented as mean (standard deviation [SD]) or median [interquartile range (IQR)] and categorical variables are presented as number (%). The incidence of POFD and mortality is presented as a 95% confidence interval (CI), calculated with the Clopper–Pearson exact test. The score of the 12-item WHODAS 2.0 is presented as median [IQR]. 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 WHODAS 2.0 score. The bootstrap procedure repeated 1,000 times was employed for internal validation, which estimated the mean odds ratio and mean area under the receiver operating characteristics curve. The 12-item WHODAS 2.0 score (median [IQR]) was described over the study period overall and was also stratified by surgical invasiveness (OSS). In a post hoc analysis, we described the WHODAS 2.0 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; R Foundation for Statistical Computing, Vienna, Austria). 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 predictor, we would need at least 3,200 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 one year follow-up, the required minimum number of cases was 4,000 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 of them lacked data on three or more items. In addition, during the follow-up process, we contacted participants twice by phone to minimize missing data.

## Results

During the study period, we identified 7,117 patients aged 55 yr and older who were scheduled to undergo elective surgery under general anesthesia. Of the 6,060 patients who met our study criteria, 4,402 patients answered the questionnaire without assistance before surgery. Surgery was postponed or canceled for 226 patients and preoperative data were missing for 156 patients. Of the 4,020 patients with complete preoperative data, 3,799 proceeded with their scheduled surgery. The follow-up rate was 76.8% (2,921/3,799) and 119 patients provided insufficient answers to the questions on the 12-item WHODAS 2.0 (119/3,799) (Fig. 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 WHODAS 2.0) and 2,921 patients (2,797 survivors and 124 deceased) were included in the analysis.

Patient characteristics are presented in Table 1. We explored the characteristics of those who were lost to follow-up *vs* those who were not (ESM, eTable 2). Several factors including younger age, restrictive lung disorders, nutritional disorders, and higher surgical invasiveness score were associated with loss to follow-up.

Reoperation was performed in 2.8% (82/2,921) of patients, and severe postoperative complications occurred in 1.7% (52/2,921) of patients (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 had multiple complications). Thirty-day mortality was 0.06% (2/2,921).

One year after surgery, 293/2,921 (10.0%; 95% CI, 8.9 to 11.1) patients experienced POFD and 124/2,921 (4.2%; 95% CI, 3.5 to 5.0) patients died. The incidence of our primary outcome was 417/2,921 (14.3%; 95% CI, 13.0 to 15.6). Of these, 390/2,921 patients had POFD (13.3%; 95% CI, 12.1 to 14.6) and 20/2,921 patients died (0.6%; 95% CI, 0.4 to 1.0) at three months, with a total incidence of 14.0% (95% CI, 12.8 to 15.3). Age, BMI ≥ 30 $kg \cdot m^{-2}$, symptomatic cerebral vascular disease, restrictive lung disease, steroid, serum albumin, nutritional status, and blood loss volume were statistically significant factors associated with POFD at one year (Table 2). 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 WHODAS 2.0 disability score after surgery, stratified by surgical invasiveness, are shown in Fig. 2 and ESM eTable 3. Patients who underwent surgeries with an OSS of 4–5 reported higher rates of disability in the 12-item WHODAS 2.0 one year after surgery than those who underwent surgeries with an OSS of 1–3 did (Fig. 2 and ESM eTable 3 and eFig. 1). The sequential changes in the 12-item WHODAS 2.0 score overall and in specific domains are shown in Table 3 and ESM eFig. 2, as well as for those who underwent joint arthroplasty ($n$ = 156). 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 one year after surgery. Our data provided some factors related to POFD and mortality, including both potentially modifiable and nonmodifiable factors. In this prospective observational study of 2,921 patients, we observed variation in the 12-item WHODAS 2.0 score at different time points, and that the majority of patients recovered to their preoperative score one year after surgery. These observations indicate that further investigation is required into the trajectory of disability after surgery.

In our cohort, 14.3% of participants experienced POFD or died one year after surgery. Although the prevalence of POFD and death one 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, including blood loss and patient-specific characteristics. Among preoperative patient characteristics, age and appropriately managed comorbidities are fixed factors that require careful perioperative management but are difficult to

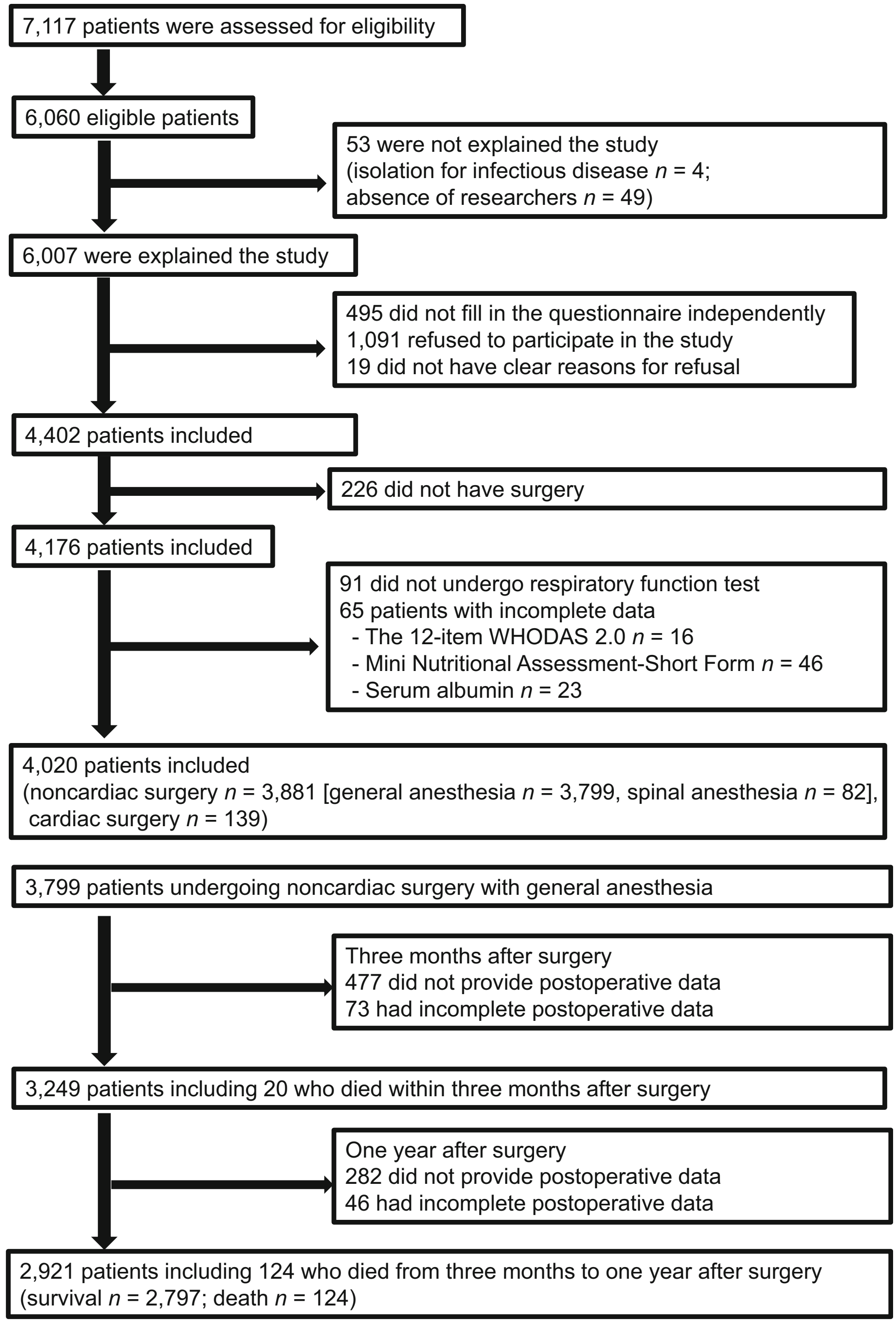


**Fig. 1** Flowchart of patient selection for noncardiac surgery with general anesthesia.

change. In contrast, potentially modifiable factors associated with 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, research into frailty—especially physical frailty—has 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

**Table 1** Demographics of patients who underwent noncardiac surgery with general anesthesia with and without postoperative functional disability or mortality

| Characteristic | Total | Presence of postoperative functional disability or mortality (+) | Absence of postoperative functional disability or mortality (-) | Mean difference (95% CI) | *P* value |
|---|---|---|---|---|---|
| | *N* = 2,921 | *N* = 417 | *N* = 2,504 | | |
| Age (yr), mean (SD) | 69.6 (7.5) | 72.6 (7.4) | 69.1 (7.4) | 3.4 (2.7 to 4.2) | <0.001 |
| Male, *n*/total *N* (%) | 1631/2,921 (55.8%) | 249/417 (59.7%) | 1,122/2,504 (44.8%) | | 0.09 |
| Body mass index ($kg \cdot m^{-2}$), 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* (%) | 189/2,921 (6.4%) | 39/417 (9.3%) | 150/2,504 (5.9%) | | |
| ≥ 18.5 to < 25, *n*/total *N* (%) | 1,879/2,921 (64.3%) | 264/417 (63.3%) | 1,615/2,504 (64.5%) | | |
| ≥ 25 to < 30, *n*/total *N* (%) | 738/2,921 (25.2%) | 89/417 (21.3%) | 649/2,504 (25.9%) | | |
| ≥ 30, *n*/total *N* (%) | 115/2,921 (3.9%) | 25/417 (6.0%) | 90/2,504 (3.6%) | | |
| Comorbidity | | | | | |
| Symptomatic cerebral vascular disease, *n*/total *N* (%) | 273/2,921 (9.3%) | 65/417 (15.5%) | 208/2,504 (8.3%) | | < 0.001 |
| Hypertension, *n*/total *N* (%) | 1.566/2,921 (53.6%) | 248/417 (59.5%) | 1,318/2,504 (52.6%) | | 0.01 |
| Ischemic heart disease, *n*/total *N* (%) | 208/2,921 (7.1%) | 45/417 (10.8%) | 163/2,504 (6.5%) | | 0.002 |
| Atrial fibrillation, *n*/total *N* (%) | 84/2,921 (2.8%) | 17/417 (4.1%) | 67/2,504 (2.7%) | | 0.15 |
| Peripheral arterial disease, *n*/total *N* (%) | 35/2,921 (1.2%) | 7/417 (1.7%) | 28/2,504 (1.1%) | | 0.46 |
| Pacemaker or defibrillator, *n*/total *N* (%) | 15/2,921 (0.5%) | 5/417 (1.2%) | 10/2,504 (0.4%) | | 0.08 |
| Asthma, *n*/total *N* (%) | 127/2,921 (4.3%) | 17/417 (4.1%) | 110/2,504 (4.4%) | | 0.87 |
| Diabetes, *n*/total *N* (%) | 548/2,921 (18.7%) | 109/417 (26.1%) | 439/2,504 (17.5%) | | < 0.001 |
| Malignant disease, *n*/total *N* (%) | 1,834/2,921 (47.3%) | 229/417 (54.9%) | 1,154/2,504 (46.0%) | | < 0.001 |
| Respiratory function | | | | | < 0.001 |
| Normal, *n*/total *N* (%) | 2,107/2,921 (72.1%) | 258/417 (61.8%) | 1,814/2,504 (72.4%) | | |
| Obstructive lung disease, *n*/total *N* (%) | 675/2,921 (23.1%) | 109/417 (26.1%) | 566/2,504 (22.6%) | | |
| Restrictive lung disease, *n*/total *N* (%) | 174/2,921 (0.59%) | 50/417 (12.0%) | 124/2,504 (5.0%) | | |
| Medication | | | | | |
| β-blocker, *n*/total *N* (%) | 186/2,921 (6.3%) | 37/417 (8.9%) | 149/2,504 (6.0%) | | 0.03 |
| Steroid, *n*/total *N* (%) | 94/2,921 (3.2%) | 30/417 (7.2%) | 64/2,504 (2.6%) | | < 0.001 |
| Statin, *n*/total *N* (%) | 536/2,921 (18.3%) | 75/417 (18.0%) | 461/2,504 (18.4%) | | 0.88 |
| Laboratory data | | | | | |
| Serum albumin ($g \cdot dL^{-1}$), 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 ($mg \cdot dL^{-1}$), 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* (%) | 1,873/2,921 (66.9%) | 213/417 (51.0%) | 1,660/2,504 (66.2%) | | |

**Table 1** continued

| Characteristic | Total | Presence of postoperative functional disability or mortality (+) | Absence of postoperative functional disability or mortality (-) | Mean difference (95% CI) | *P* value |
|---|---|---|---|---|---|
| At risk of malnutrition, *n*/total *N* (%) | 912/2,921 (31.2%) | 166/417 (39.8%) | 746/2,504 (29.8%) | | |
| Malnutrition, *n*/total *N* (%) | 136/2,921 (4.6%) | 38/417 (9.1%) | 98/2,504 (3.9%) | | |
| Preoperative 12-item WHODAS 2.0 score, mean (SD) | 14.5 (17.5) | 23.9 (18.8) | 13.0 (16.8) | 10.9 (9.1 to 12.6) | < 0.001 |
| Anesthetic drug | | | | | < 0.001 |
| Propofol, *n*/total *N* (%) | 827/2,921 (28.3%) | 89/417 (21.3%) | 738/2,504 (29.4%) | | |
| Inhalation agents, *n*/total *N* (%) | 2,094/2,921 (71.6%) | 328/417 (78.6%) | 1,766/2,504 (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* (%) | 2,080/2,921 (71.2%) | 252/417 (60.4%) | 1,828/2,504 (73.0%) | | |
| 100–499, *n*/total *N* (%) | 629/2,921 (21.5%) | 120/417 (28.8%) | 509/2,504 (20.3%) | | |
| ≥ 500, *n*/total *N* (%) | 212/2,921 (7.2%) | 45/417 (10.8%) | 167/2,504 (6.7%) | | |
| Operative stress score | | | | | 0.003 |
| 1, *n*/total *N* (%) | 204/2,921 (6.9%) | 27/417 (6.5%) | 177/2,504 (7.1%) | | |
| 2, *n*/total *N* (%) | 822/2,921 (28.1%) | 98/417 (23.5%) | 724/2,504 (28.9%) | | |
| 3, *n*/total *N* (%) | 1,214/2,921 (41.5%) | 168/417 (40.3%) | 1,046/2,504 (41.8%) | | |
| 4, *n*/total *N* (%) | 530/2,921 (18.1%) | 90/417 (21.6%) | 440/2,504 (17.6%) | | |
| 5, *n*/total *N* (%) | 151/2,921 (5.1%) | 34/417 (8.2%) | 117/2,504 (4.7%) | | |

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

are needed to identify strategies to improve preoperative malnutrition, and whether these interventions improve patient-reported outcomes, including POFD.

We assessed the sequential score of the 12-item WHODAS 2.0; however, the median scores shown in this study were not able to capture the presence of different trajectories of functional recovery after surgery as some cases were associated with improved function and others with decreased function. In general, we observed considerable variability within subgroups of patients in our study, even when considering only joint arthroplasty. In the future, a larger study is needed to understand functional disability after specific surgeries.

In our cohort, the incidences of complications and mortality after surgery were relatively low. This may be due to several factors: 1) 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] 2) 76.5% of the surgeries were of lower invasiveness (OSS 1–3), and 3) 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 patient

**Table 2** Multiple logistic regression analysis for predicting patients with postoperative functional disability or mortality at one year after surgery

| | Odds ratio (99.5% CI) | *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 to < 25 | 1 | |
| ≥ 25 to<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 | | |
| Beta 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$^{-1}$) | 0.55 (0.35 to 0.85) | < 0.001 |
| Serum creatinine (mg·dL$^{-1}$) | 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 |

CI = confidence interval; NA = not available

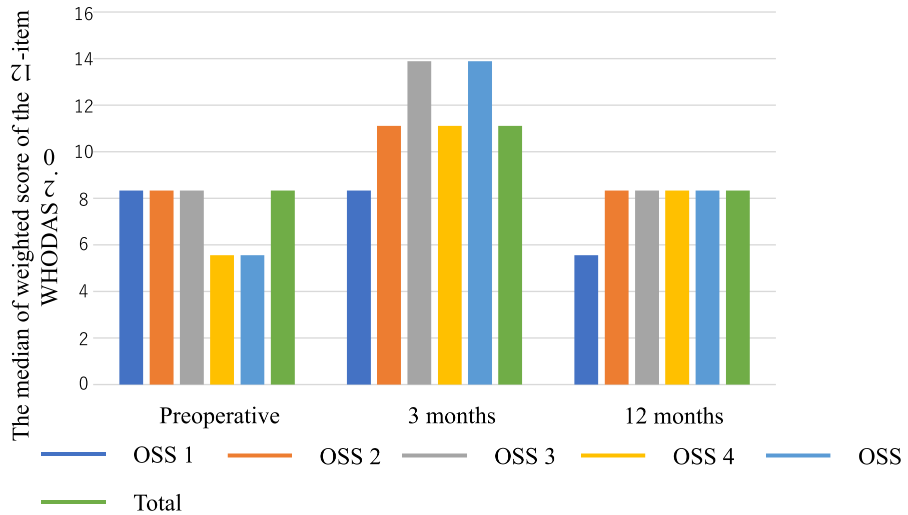


**Fig. 2** The sequential changes in the 12-item World Health Organization Disability Assessment Schedule (WHODAS) 2.0 score stratified by the Operative Stress Score in patients who underwent noncardiac surgery with general anesthesia. The 12-item WHODAS 2.0 score in patients who underwent surgeries with an operative stress score of 2 and in overall patients followed the same trajectory; therefore, the graph shows the overall trend.

optimization in our preoperative assessment clinics before surgery.

Our study has several limitations. First, this study included only patients who underwent surgery and were able to complete 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 one year is shown in ESM eTable 2, 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 is unclear; however, the incidence of 14.3% may be underestimated because some covariates were also associated with POFD. This suggests that missing data may not have occurred at random and may have introduced bias. Second, we only examined the predictive performance of our model and did not assess the external validity. Third, postoperative functional status is affected by factors other than those evaluated in this study. Finally, the generalizability of our findings may be limited because this was a single-center study.

In conclusion, in a large-scale prospective observational study, we found that one in seven patients aged $\geq$ 55 yr who underwent elective noncardiac surgery with general anesthesia experienced POFD or mortality one year postoperatively, and that 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.

**Table 3** Sequential changes in the 12-item World Health Organization Disability Assessment Schedule 2.0 score on the specific domains in the overall cohort and in a subset of patients who had hip or knee arthroplasty

| | | Preoperative Median [IQR] | Three months Median [IQR] | One year Median [IQR] |
|---|---|---|---|---|
| All patients | | | | |
| $N$ = 2,797 | | | | |
| 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] |
| Hip or knee arthroplasty patients | | | | |
| $N$ = 156 | | | | |
| 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] |

Each item has a score between 0 and 4. The total score is converted to percentage using the formula, (sum score/48) × 100

IQR = interquartile range

**Author contributions** *Mitsuru Ida* and *Masahiko Kawaguchi* had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis. *Mitsuru Ida* and *Masahiko Kawaguchi* contributed to study concept and design. *Mitsuru Ida*, *Yuu Tanaka*, and *Masahiko Kawaguchi* contributed to acquisition, analysis, or interpretation of data. *Mitsuru Ida* contributed to drafting of the manuscript. *Mitsuru Ida* and *Yuu Tanaka* contributed to statistical analysis. *Masahiko Kawaguchi* obtained funding. *Yuu Tanaka* and *Masahiko Kawaguchi* provided administrative, technical, or material support. *Satoki Inoue* and *Masahiko Kawaguchi* contributed to *s*upervision. All authors contributed to critical revision of the manuscript for important intellectual content.

**Acknowledgements** We would like to thank Editage (www.editage.com) for English language editing. Hisako Yoshida (Department of Medical Statistics, Osaka City University Graduate School of Medicine, Osaka, Japan), Kanae Takahashi (Department of Medical Statistics, Osaka City University Graduate School of Medicine, Osaka, Japan) advised and assisted in statistical planning and analysis.

**Disclosures** None.

**Funding statement** This study was funded by a grant from Nara Prefecture: "Nara Medical University Grant-in-Aid for a large-scale prospective cohort study on healthy life expectancy." Role of the funding source: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Editorial responsibility** This submission was handled by Dr. Alana M. Flexman, Associate Editor, *Canadian Journal of Anesthesia/Journal canadien d'anesthésie.*

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