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Worse ECOG-PS Is Associated with Increased 30-Day Mortality among Adults Older than 90 Years Undergoing Non-Cardiac Surgery: A Single-Center Retrospective Study

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Background: A growing number of older patients are undergoing surgeries. However, reliable preoperative predictors of surgical mortality among older patients have not been identified. This study compared predictive factors for 30-day survival in patients older than 90 years after non-cardiac surgery.
Methods: This retrospective study at Nippon Medical School Hospital investigated the records of patients aged >90 years who underwent non-cardiac surgeries between 2010 and 2020. The data collected included age, gender, American Society of Anesthesiologists physical status (ASA-PS), preoperative Charlson score, preoperative fall risk assessment, Eastern Cooperative Oncology Group performance status (ECOG-PS), modified 5-item frailty index (mFI-5), need for intraoperative transfusion, postoperative complications, and 30-day survival after surgery.
Results: A total of 327 cases of elective surgery and 149 cases of emergency surgery were examined. Nonsurvivors (n=20, 4.2%) had significantly worse preoperative ASA-PS (for emergency cases) (nonsurvivors vs. survivors, 2.8 [2-3] vs. 2.3 [1-4], p=0.045), ECOG-PS (3.0 [2-4] vs. 1.0 [0-4], p<0.001), and mFI-5 values (3.0 [1-4] vs. 1.0 [0-3], p<0.001), more emergency cases (75.0% vs. 36.2%, p=0.004), and a greater need for intraoperative transfusion (55.0% vs. 13.4%, p<0.001). Among frailty assessment methods, ECOG-PS was the most strongly associated with 30-day mortality (area under the curve, ECOG-PS: 0.98, p<0.001; mFI-5: 0.86, p<0.001; Charlson score: 0.53, p=0.71; fall risk assessment: 0.55, p=0.44). Kaplan-Maier curves and multivariate logistic regression analysis demonstrated that an ECOG-PS of >3 was significantly associated with 30-day mortality (ECOG-PS: Kaplan-Maier curve, p<0.001, Log-rank test; odds ratio 1.71, 95% confidence interval: 1.35-2.16, p<0.001).
Conclusions: An ECOG-PS of >3 was significantly correlated with 30-day mortality after non-cardiac surgery in patients older than 90 years. (J Nippon Med Sch 2022; 89: 295–300)

Key words: older patient, frailty, perioperative characteristic, postoperative complication, surgical outcome

Introduction

In Japan, older adults often undergo surgical treatment, even those older than 90 years. In 2021, 2.0% of the population of Japan was >90 years old[1], and they are able to undergo minimally invasive surgeries because of advances in medical technology. These surgeries are especially useful for patients with compromised health, such as older patients and high-risk patients. Older patients undergoing standard surgeries are at higher risk than younger patients undergoing similar surgeries[2,3]. Some perioperative management guidelines recommend using intensive patient monitoring and multimodal pain management for older patients[4,5]. Several studies have analyzed preoperative risk factors for mortality among older patients, using assessment tools including American Society of Anesthesiologists physical status (ASA-PS), the rate of preoperative complications, the Charlson score[6], the fall risk assessment[7], the modified 5-item frailty index (mFI-5)[8], and the Eastern Cooperative Oncology Group performance status (ECOG-PS)[9]. Frailty is a key factor in perioperative management of older patients, but with respect to patients aged >90, data on optimal

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assessment methods or scales are limited. No previous Japanese report has focused on predictors of surgical mortality among the old-old, but such predictors are essential as a basis for preoperative evaluation and informed consent. Therefore, this study analyzed perioperative patient characteristics and mortality to identify reliable preoperative predictors of mortality among patients older than 90 years undergoing non-cardiac surgery.

Materials and Methods

In this retrospective study, we collected data (from medical and anesthesia records) for adults aged >90 years who had received any type of anesthesia for non-cardiac surgery at Nippon Medical School Hospital between April 2010 and December 2020. This study was approved by the Ethics Committee of Nippon Medical School Hospital, Bunkyo, Tokyo, Japan, on 18 December 2020 (no. B-2020-236). An opt-out recruitment of participants was available for patients aged >90 years who had received any type of anesthesia for non-cardiac surgery at Nippon Medical School Hospital between April 2010 and December 2020. Patients who underwent multiple surgeries during the same hospital stay were excluded from the study.

The variables analyzed were age, gender, body mass index (BMI), ASA-PS, preoperative Charlson score[6], the preoperative fall risk assessment[7], mFI-5[8], ECOG-PS[9], type of anesthesia, indication(s) for surgery, surgery site, duration of anesthesia, duration of surgery, volume of fluid administered during surgery, volume of blood loss, need for intraoperative transfusion (red cell concentrates, fresh frozen plasma, platelets, and albumin), use of an electroencephalogram monitor, duration of hospital stay, postoperative complications (hypoxia, delirium diagnosed by psychiatrists, and aspiration pneumonia), and 30-day survival after surgery. Hypoxia was defined as oxygen saturation (SpO_2) under 95% in room air after surgery, and aspiration pneumonia defined as a newly diagnosed pneumonia after surgery, with an episode of vomiting or aspiration. Presence of postoperative delirium was determined on the basis of recorded symptoms or a psychiatrist diagnosis. We classified patients by surgical outcome as nonsurvivors and survivors. Emergency and elective cases were examined in subgroup analysis.

Statistical Analysis

All numerical data are expressed as median (range). Differences between survivors and nonsurvivors, and between emergency and elective procedures, were assessed by the Mann-Whitney test or chi-square test using Prism ver. 5.0 software (GraphPad Software, La Jolla, CA, USA) unless otherwise specified, and receiver operating characteristic (ROC) curves of the sensitivity for mortality of preoperative assessments were drawn with the same software. The cut-off threshold for ROC curves was set to maximize sensitivity and specificity (Youden's index). Multivariate logistic regression analysis, Wilcoxon analysis, and Kaplan-Maier curves were performed using JMP ver. 11.0 (SAS Institute, Tokyo). Multivariate logistic regression analysis was used to identify preoperative factors associated with 30-day survival after emergency surgery. Two explanatory variables, one per 10 survivors, were applied to multivariate logistic regression analysis, namely, abdominal surgery and ECOG-PS >3. ECOG-PS was selected from among the preoperative frailty assessments, and abdominal surgery was selected from among the other preoperative factors. Statistical significance was set at a p-value of <0.05.

Results

The cohort of 476 patients aged >90 years was 0.6% of the 79,860 surgical patients requiring anesthesia at our hospital during the study period. Among these, 327 patients underwent elective surgeries and 149 underwent emergency surgeries.

Perioperative Conditions of Nonsurvivors and the Survivors

The characteristics of the patients are summarized in **Table 1**. Among the 476 patients, 20 (4.20%) died within 30 days after non-cardiac surgery. Age, gender, and BMI were similar between survivors and nonsurvivors, but nonsurvivors were significantly more likely to undergo emergency surgery (36.2% vs. 75.0%, p=0.004) and to require preoperative ventilation (2.4% vs. 20%, p=0.004).

The distribution of surgery sites was similar in nonsurvivors and survivors. The respective values were as follows: head/neck, 20.0% vs. 9.65%; abdomen, 65.0% vs. 42.5%; extremities, 15.0% vs. 33.9%; and superficial, 0.0% vs. 8.99% (p = 0.058, chi-square test). General anesthesia was required by most nonsurvivors and survivors (85.0% vs. 84.6%, p=1.00), but postoperative ventilation was more often required by nonsurvivors (40.0% vs. 3.29%, p <0.001).

Postoperative complications developed in 66 patients (13.9%): 5 nonsurvivors (25.0%) and 61 survivors (13.9%) (p=0.17). There were no significant differences in the incidence of postoperative complications, except for hypoxia (nonsurvivors, 40.0% vs. survivors, 2.41%, p<0.001). Du-

Table 1 Preoperative and intraoperative patient characteristics

	Nonsurvivors	Survivors	p-value
Patient characteristics			
Patients, n (%)	20 (4.20)	456 (95.8)	–
Age, median, [IQR]	92.3 [90–98]	92.4 [90–102]	0.83
Female/male, n (%)	12 (60.0)/8	293 (64.3%)/163	0.81
BMI, median [IQR]	20.5 [13.7–23.8]	20.8 [12.3–32.5]	0.73
Emergency surgery, n (%)	14 (70.0)	135 (29.6)	0.003
ASA-PS, 1/2/3/4/5, n (%)	0/1 (5.0)/5 (25.0)/0/0	5 (1.1)/203 (44.5)/112 (24.6)/1 (0.2)/0	0.11
1E/2E/3E/4E/5E, n (%)	0/4 (20.0)/11 (55.0)/0/0	0/74 (16.2)/49 (10.8)/10 (2.2)/2 (0.4)	0.045
Charlson score, median [IQR]	2.4 [0–4]	2.3 [0–7]	0.93
Fall risk assessment, I/II/III, n (%)	2 (10.0)/12 (60.0)/6 (30.0)	68 (15.0)/286 (62.7)/102 (22.4)	0.67
ECOG-PS, 0/1/2/3/4, n (%)	0/0/3 (1.5)/10 (50.0)/7 (3.5)	225 (49.3)/180 (39.5)/39 (8.6)/11 (2.4)/1 (0.2)	<0.001
mFI-5, 0/1/2/3/4, n (%)	0/3 (15.0)/4 (20.0)/11 (55.0)/1 (5.0)	103 (22.6)/214 (46.9)/128 (28.1)/10 (2.2)/1 (0.2)	<0.001
Preoperative ventilation, n (%)	4 (20.0)	13 (2.9)	0.004
Intraoperative characteristics			
Surgical site, n (%)			0.058
Head/neck	4 (20.0)	44 (9.7)	
Abdominal	13 (65.0)	194 (42.5)	
Extremity	3 (15.0)	155 (34.0)	
Superficial	0	41 (9.0)	
Other	0	22 (4.8)	
General anesthesia, n (%)	17 (85.0)	386 (84.7)	1.000
Anesthesia time, min, median [IQR]	225 [92–375]	186 [23–769]	0.05
Surgery time, min, median [IQR]	159 [59–326]	115 [6–635]	0.01
Fluid volume, mL, median [IQR]	3,215 [430–7,760]	1,243 [100–5,100]	<0.001
Volume of blood loss, mL, median [IQR]	464.3 [0–3,910]	86.7 [0–1,431]	<0.001
Need for transfusion, n (%)	11 (55.0)	61 (13.4)	<0.001
Urine, mL, median [IQR]	319.3 [5–1,150]	164.6 [0–1,900]	0.008
EEG monitor, n (%)	6 (30.0)	124 (27.2)	0.80
Postoperative ventilation, n (%)	8 (40.0)	15 (3.3)	<0.001
Postoperative results			
Perioperative complications, n (%)	5 (25.0)	61 (13.4)	0.18
Delirium	1 (5.0)	39 (8.6)	1.00
Aspiration pneumonia	0	4 (0.9)	1.00
Hypoxia	8 (40.0)	11 (2.4)	<0.001
Cerebral infarction	0	4 (0.9)	1.00
Ventilation-associated pneumonia	1 (5.0)	0	1.00
Shunt occlusion	0	1 (0.2)	1.00
Congestive heart failure	1 (5.0)	0	1.00
Infection	0	1 (0.2)	1.00
Length of hospital stay, days, median [IQR]	12.5 [0–30]	21.0 [2–147]	0.047

Data are shown as patient number (%) or median [range].
BMI: body mass index; ECOG-PS: Eastern Cooperative Oncology Group performance status; mFI-5: Modified 5-item Frailty Index; ASA-PS: American Society of Anesthesiologists physical status; EEG: electroencephalogram.

ration of hospital stay was significantly shorter for nonsurvivors than for survivors (12.5 vs. 21.0 days, p=0.047).

Risk Factors for Surgical Mortality

Regarding the preoperative assessment scales, the ASA-PS, ECOG-PS, and mFI-5 showed significant differences between nonsurvivors and survivors, but the Charlson score and fall risk assessment did not (ASA-PS: 2.8 [2-3] vs. 2.3 [1-4], p=0.11; ASA-PS E: 2.8 [2-3] vs. 2.3 [1-4], p=0.045; ECOG-PS: 3.0 [2-4] vs. 1.0 [0-4], p<0.001; mFI-5: 2.5 [1-4] vs. 1.0 [0-3], p<0.001; Charlson score: 2.4 [0-4] vs. 2.3 [0-8], p=0.93; fall risk assessment: 2.2 [1-3] vs. 2.0 [1-3], p=0.67; Mann-Whitney test). To identify an efficient preoperative assessment method, we compared ROC curves of the sensitivities of the preoperative assessments for 30-day mortality (**Fig. 1**).

The area under the curve (AUC), p-values, and cut-off thresholds with sensitivity and specificity are summarized in **Table 2**.

Association of Need for General Anesthesia with Mortality after Emergency Surgery

Subgroup analysis was performed to clarify the association between emergency surgery and ECOG-PS. The emergency group had significantly worse ECOG-PS than the elective group (p<0.001, chi-square test), including severe multiple organ dysfunction (i.e., renal dysfunction requiring hemodialysis, catecholamine use, arrhythmia, and preoperative ventilation). Thus, additional analysis was performed of the emergency and elective groups. We analyzed preoperative factors that significantly differed in the characteristic analysis (i.e., abdominal surgery and ECOG-PS) by using multivariate logistic regression analysis of 30-day survival after emergency surgery (**Table 3**). That analysis revealed, among emergency cases, a significant association between 30-day mortality and an ECOG-PS >3 (odds ratio [OR] 1.71, 95% confidence interval [CI]: 1.35-2.16, p<0.001) and abdominal surgery (OR: 9.38, 95% CI: 1.01-86.73, p=0.049). Kaplan-Maier curves showed that a worse ECOG-PS was significantly associated with worse 30-day survival among emergency and elective cases (ECOG-PS, p<0.001; emergency group, p<0.001; elective group, p<0.001; **Fig. 2**).

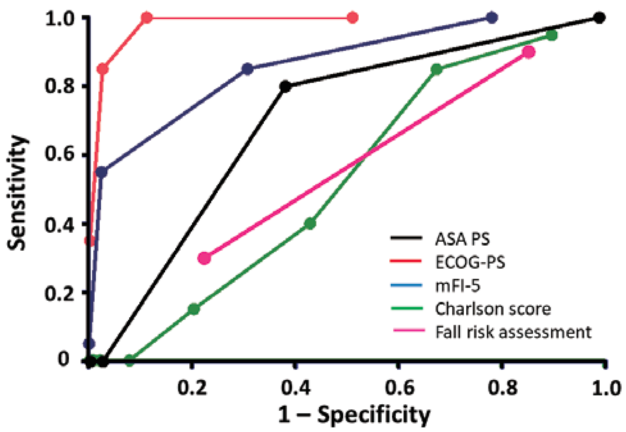

Fig. 1 ROC curves of preoperative assessments for 30-day mortality.
ASA PS: American Society of Anesthesiologists physical status; ECOG-PS: Eastern Cooperative Oncology Group performance status; mFI-5: modified 5-item frailty index.

Discussion

This retrospective study analyzed risk factors associated with 30-day mortality after non-cardiac surgery among patients aged >90 years. Data from 476 patients were analyzed, including 149 emergency surgery cases (31.3%), and the overall survival rate was 95.8%. Comparison of ROC curves showed that ECOG-PS was the best preoperative predictor of 30-day mortality. The results of multivariate regression analysis indicated that an ECOG-PS >3 was independently associated with 30-day mortality, especially after emergency surgery.

Frailty, as evaluated by the ECOG-PS and mFI-5 and other assessment tools, is associated with surgical outcomes for adults[9–11]. Especially among older patients, preoperative and/or postoperative frailty and comorbidity are predictors of mortality, as are functional evaluation scales[12,13]. In 1996, the ASA-PS was reported to be a predictor of surgical outcomes for all age groups[14]. The optimal methods for evaluating frailty (especially in older patients) have been discussed for many years. Frailty evaluations vary greatly and include fall risk assessments[7], the ECOG-PS[9], and the mFI-5[8]. The ECOG-PS was originally developed to evaluate cancer patients and simply consisted of the bed-based time ratio in patient's daily life. It was reported to be independently associated with postoperative 30-day mortality in a cohort of high-risk emergency surgery patients[9]. A large comparative study including patients of all age groups reported that

Table 2 ROC curve results in preoperative assessments

Assessment methods	AUC	Threshold	Sensitivity	Specificity	p-value
ASA-PS	0.70	2.5	0.80	0.62	0.003
ECOG-PS	0.98	2.5	0.85	0.98	<0.001
mFI-5	0.86	1.5	0.85	0.69	<0.001
Charlson score	0.53	1.5	0.85	0.33	0.77
Fall risk assessment	0.55	2.5	0.30	0.78	0.44

AUC: Area under the curve; ASA-PS: American Society of Anesthesiologists physical status; ECOG-PS: Eastern Cooperative Oncology Group performance status; mFI-5: modified 5-item frailty index.

Table 3 Multivariate logistic regression analysis of 30-day mortality among older patients after emergency non-cardiac surgery

Variable	Odds ratio [95%CI]	p-value
Abdominal surgery	9.38 [1.01-86.73]	0.049
Preoperative ECOG-PS >3	1.71 [1.35-2.16]	p<0.001

ECOG-PS: Eastern Cooperative Oncology Group performance status.

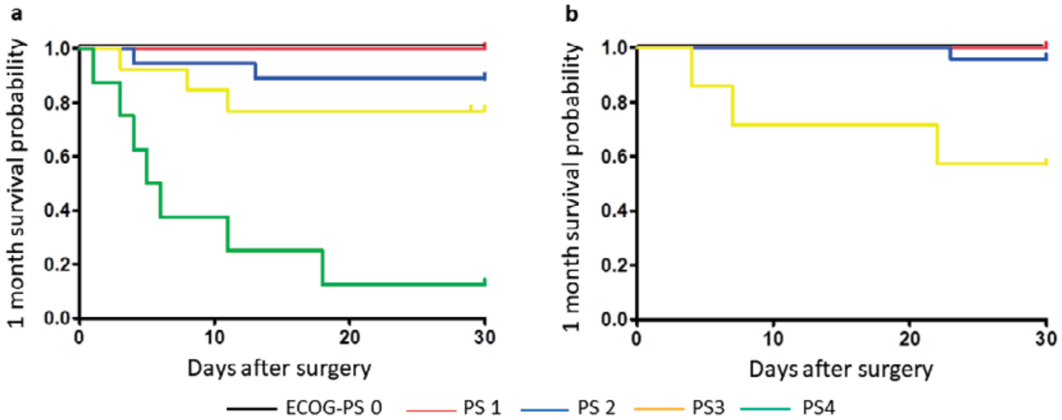

Fig. 2 Kaplan–Meier curves up to postoperative day 30. a: Kaplan–Meier curves for ECOG-PS up to 30 days after emergency surgery (n = 149, p<0.001 Log-rank test). b: Kaplan–Meier curves for ECOG-PS up to 30 days after elective surgery (n = 327, p<0.001 Log-rank test).
ECOG-PS: Eastern Cooperative Oncology Group performance status.

mFI-5 and mFI-11 were effective in predicting surgical outcomes[15] and postoperative complications[16]. When the analysis is limited to patients aged >90, there is no consensus on predictors of postoperative mortality. Our present study was limited to patients aged >90 and is the first to compare the efficiency of frailty assessments. Our findings indicate that the ECOG-PS is the most efficient tool for estimating 30-day mortality in this patient population, especially for emergency cases. Our data indicate that, in frailer patients, disease symptoms such as cholecystitis or colorectal emergency tend to be missed early because patients are unable to inform their caregiver or family, thus possibly leading to disease progression.

The present 30-day mortality and postoperative complication rates were lower than those in previous reports, and there was no association between delirium and 30-day mortality. Several studies analyzed risk factors for postoperative mortality among older patients, but few enrolled patients aged ≥90 years. Studies of patients aged ≥80 years reported 8-10% mortality at 30 days after non-cardiac surgery[17,18], a 50% rate of postoperative dysfunction, and a 20-32% rate of postoperative complications[17,19]. Some studies of patients aged ≥75 years reported that postoperative delirium, which was present in 36% of the patients, was associated with increased mortality, institutionalization, and dependency but not with increased risk of re-admission during follow-up[20]. These differences are likely attributable to adequate preoperative evaluations, appropriate patient monitoring, advances in surgical treatment or anesthetic, or early detection of postoperative complications.

This retrospective analysis of 476 geriatric patients showed that a worse ECOG-PS was independently associated with 30-day mortality. However, our study has limitations. It was a retrospective analysis of a single racial group at a single center. No previous Japanese report studied a large population of patients aged >90 or examined predictive factors of surgical mortality among the old-old. Surgical indications for old-old patients, especially emergency cases, could differ in relation to country, cultural background, and availability of medical resources. In addition, we evaluated only patient anesthesia and medical records; thus, other potential complications may have been missed. Dementia, delirium, and other postoperative complications might be included if other definitions of postoperative complications are used. Our present findings are still meaningful, however, because of the relatively large number of patients aged >90 years, and can serve as the basis for preoperative evaluation and informed consent. Nevertheless, a prospective international multicenter study with larger numbers of such patients is necessary.

Conclusion

The present study analyzed factors predicting 30-day mortality after non-cardiac surgery for 476 patients aged >90 years. Preoperative ECOG score should be considered a predictor of mortality, especially for patients undergoing emergency surgery.

Conflict of Interest: None declared.

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