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# Pancreaticoduodenectomy for octogenarians under postoperative rehabilitation enhanced ERAS protocol

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## Abstract

**Background** Although pancreaticoduodenectomy (PD) for pancreatic or periampullary cancer is the gold standard treatment regardless of patient age, patients aged 80 years or older have poor postoperative short-term outcomes because of their poor functional status and many medical comorbidities. Postoperative rehabilitation in octogenarians could improve postoperative outcomes; however, its effect remains unclear.

**Methods** This retrospective study included patients who underwent PD at two institutions between January 2019 and December 2022. All patients were managed using the enhanced recovery after surgery (ERAS) protocol, and elderly patients or those with loss of muscle mass or frailty underwent additional perioperative rehabilitation. Postoperative short-term outcomes were compared between the octogenarians and non-octogenarians.

**Results** We reviewed 251 patients including 44 octogenarians (17.5%). Octogenarians had higher rates of comorbidity (78.9% vs. 55.1%, $P=0.049$) and sarcopenia (31.8% vs. 16.4%, $P=0.018$) and a more impaired nutritional status than non-octogenarians and received postoperative rehabilitation more frequently (86.4% vs. 44.0%, $P<0.001$, respectively). Under the rehabilitation-enhanced ERAS protocol, the postoperative major complication rate (25.0% vs. 24.6%, $P=0.960$), the length of hospital stay (LOS) ($P=0.435$), and the length of functional recovery (LOFR) ($P=0.110$) did not differ between the two groups. In the multivariate analysis, age ≥ 80 years was not determined as a risk factor for major complications.

**Conclusions** Despite the poor functional and nutritional status of octogenarians, their postoperative major complication rates, LOS, and LOFR after PD were comparable with those of non-octogenarians under the rehabilitation-enhanced ERAS protocol.

**Keywords** Sarcopenia, Pancreaticoduodenectomy, Octogenarians, Rehabilitation

## Introduction

In recent years, society has been aging, and the percentage of elderly people over 80 years of age in 2022 was reported to be 3.2% worldwide, 6.5% in North America, and 18.2% in Japan [1]. These percentages are expected to increase to 7.9%, 17.2%, and 29.5%, respectively, by 2050, and the number of octogenarians undergoing surgery is also expected to increase. Japan's population is aging faster than other countries, and the percentage of octogenarians among patients undergoing surgery has

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increased from 10.2% to 14.6% between 2011 and 2019 [2]. Other countries will experience similar percentage increases in the future.

Several studies have shown that the oncological benefit of pancreaticoduodenectomy (PD) in patients with pancreatic or periampullary cancer is similar between octogenarians and younger patients; therefore, PD is a standard treatment regardless of patient age [3–8]. Despite advances in surgical techniques and management, PD remains a highly invasive procedure with the potential to develop serious postoperative complications [9–11]. Moreover, elderly patients have impaired organ function, physical condition, and many medical comorbidities. Therefore, the feasibility of PD should be carefully evaluated in older patients. According to a meta-analysis, patients aged 80 years or older have a high rate of postoperative complications, long length of hospital stay (LOS), 30-day mortality, and their poor functional status and medical comorbidities rather than age itself contribute to increased postoperative morbidity and mortality after PD [12–14].

In addition to other comorbidities, sarcopenia has also been reported as a risk factor for high morbidity and mortality after pancreatic resection in patients aged 65 years or older [15]. Sarcopenia is a syndrome characterized by progressive loss of lean skeletal muscle mass and strength, and its prevalence increases with age [16]. To minimize the disadvantages in elderly patients, the early and scheduled mobilization could be beneficial; however, there is little evidence in the literature [17]. Furthermore, there is a general reluctance among pancreatic surgeons to induct ERAS protocols for elderly patients undergoing pancreatoduodenectomy, citing safety concerns. Therefore, in this study, we aimed to evaluate whether an ERAS protocol with additional postoperative rehabilitation improves postoperative short-term outcomes in patients aged ≥ 80 years undergoing PD.

## Methods

This study was performed at the Department of Hepatobiliary-Pancreatic Surgery, Juntendo University Hospital and the Department of General Surgery, Juntendo University Nerima Hospital. The Juntendo University Hospital Review Board approved the study protocol (E23-0315-N01). A retrospective review of electronic medical health records was performed for patients who underwent PD at two institutions between January 2019 and December 2022. The institutional review board waived the need for informed consent to be obtained from patients for the use of their medical, imaging, or pathology records. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. Patients who underwent robotic, laparoscopic, or emergent surgeries were excluded. Patients who underwent simultaneous organ resection such as hepatic resection, colorectal resection, or esophagectomy were also excluded.

### Preoperative CT scan measurements and preoperative evaluation tests

We measured the preoperative skeletal muscle area (SMA) at the third lumbar vertebra (L3) using the SYNAPSE VINCENT software (version 4.0; Fujifilm Medical, Tokyo, Japan) or ITK-SNAP software (http://www.itksnap.org/pmwiki/pmwiki.php). The skeletal muscle index (SMI) was calculated by dividing the SMA at the L3 vertebral body ($cm^2$) by the height (m) squared. Patients were diagnosed with sarcopenia when their SMI were less than the cut-off values (37.9 $cm^2/m^2$ for male and 28.6 $cm^2/m^2$ for female) [18]. In addition, the patients underwent preoperative examination for cardiovascular and pulmonary function, regardless of age. Octogenarians did not routinely undergo supplemental examinations.

### Surgical procedure

Subtotal stomach-preserving PD (SSPPD) or pylorus-preserving PD (PPPD) was performed depending on the tumor type and surgeon's decision. When the tumor was in contact with the portal vein or superior mesenteric vein on preoperative CT images, PV/SMV vein resection was performed [19].

### ERAS pathway and rehabilitation

All the patients were managed using the ERAS protocol [17]. Under our ERAS protocol, patients started water intake at postoperative day (POD) 1, solid diet (20–25 kcal/kg/day) on POD 3, and solid diet (25–30 kcal/kg/day) on POD 5. Fluid overload in the patients was avoided both intraoperatively and postoperatively. Glucose levels were controlled in all patients. No nasogastric tubes were placed. The urinary catheter was removed POD 4. Drains were removed on POD 4 if patients did not develop biochemical leakage according to the International Study Group of Pancreatic Surgery (ISGPS) definition. Additionally, we used a combination of epidural anesthesia, intravenous analgesics, and oral painkillers and encouraged patients to mobilize from POD 1. Perioperative rehabilitation was introduced in elderly patients or those with loss of muscle mass or frailty, at the discretion of the attending surgeon. Basically, patients older than 75 years or those with an Eastern Cooperative Oncology Group performance status of ≥ 2 received rehabilitation. Rehabilitation mainly included aerobic exercise, for at least 40 min from POD 1. Gait training was performed,

if possible. Otherwise, patients underwent muscle training to prevent disuse. Activity levels were assessed daily by physical therapists, and the intensity of the rehabilitation program and the daily target were individualized by physical therapists and changed based on the recovery of the patients' physical condition. In standard protocol, patients were expected to walk 20 m on POD 1 and 80 m on POD 2. Patients in serious general condition because of postoperative complications received exercise on bed to prevent contractures, and the intensity of exercise was increased according to the recovery of their general condition. We checked whether patients actually received rehabilitation or not by reviewing the medical records of the physical therapists.

Patients who were admitted to hospitals a week before surgery for glycemic control received preoperative rehabilitation to prevent disuse. The indications depended on the surgeon's discretion. Preoperative rehabilitation consisted of aerobic and resistance exercises, and the intensity depended on the physical functional status.

### Data collection

Demographic data including age, sex, diagnosis, history of treatment, American Society of Anesthesiologists physical status (ASA), history of comorbidities such as diabetes mellitus and hypertension, and smoking habits were recorded. Preoperative blood samples were collected within two weeks before surgery, and nutritional status was assessed using the prognostic nutritional index (PNI), controlling nutritional status score (CONUT), Glasgow prognostic score (GPS), nutrition risk screening tool (NRS2002), and Mini Nutritional Assessment Short Form (MNA-SF) [20–25]. Perioperative rehabilitation treatment, history of perioperative chemotherapy, and intraoperative findings were also recorded.

All postoperative complications were classified using the Clavien-Dindo classification. Postoperative pancreatic fistula (POPF) was classified according to ISGPS criteria [26]. Delayed gastric emptying (DGE) was defined according to ISGPS definitions. Failure to rescue has been defined as the inability to prevent death within 90 days after surgery after the development of a complication [11, 27]. LOS, length of functional recovery (LOFR), and 90-day mortality were also obtained from the medical records [28].

### Statical analysis

The entire cohort was divided into two groups: patients aged ≥ 80 years (octogenarians) and those aged ≤ 79 years (non-octogenarians). The clinical characteristics and postoperative outcomes between the two groups were compared using the chi-square test or Fisher's exact test for non-continuous variables and the Mann–Whitney U-test for continuous variables. Continuous variables are reported as medians with ranges. Major complications were defined as complications greater than grade IIIa according to the Clavien-Dindo classification. Variables with $P < 0.10$ in univariate analysis and previously reported factors associated with major complication rate were entered into multivariate logistic regression analysis to determine risk factors for major complications. *P* values of less than 0.05 were regarded as denoting statistically significant differences. Binomial logistic regression analysis was used to determine the odds ratios (ORs) with 95% confidence intervals (CI). All analyses were performed using the IBM SPSS Statistics 21 software package (SPSS Inc., Tokyo, Japan).

## Result

### Patient characteristics

We reviewed 251 patients including 44 octogenarians (17.5%). The BMI and ASA levels were not different between the two groups (Table 1). Octogenarians had a higher proportion of cholangiocarcinoma (43.2% vs. 12.1%, $P < 0.001$) and a lower rate of preoperative chemotherapy than non-octogenarians (20.5% vs. 44.4%, $P = 0.004$). The rate of having at least one comorbidity was higher in octogenarians than in non-octogenarians (78.9% vs. 55.1%, $P = 0.049$). The comorbidity rates of hypertension (61.4% vs. 32.4%, $P < 0.001$) and cerebrovascular accidents (15.9% vs. 3.8%, $P = 0.007$) were higher in the octogenarians. Octogenarians had significantly lower serum albumin levels ($P < 0.001$) and worse PNI ($P = 0.005$), GPS ($P < 0.001$), MNA-SF ($P = 0.009$), and NRS2002 ($P < 0.001$) scores than non-octogenarians (Table 2).

### Sarcopenia and rehabilitation

The octogenarian group had a higher rate of sarcopenia (31.8% vs. 16.4%, $P = 0.018$) and received peri- and post-operative rehabilitation more frequently than the non-octogenarian group (15.9% vs. 4.8%, $P = 0.016$ and 86.4% vs. 44%, $P < 0.001$, respectively) (Table 2). Similarly, patients diagnosed with sarcopenia received peri- and post-operative rehabilitation more frequently (16.7% vs. 4.4%, $P = 0.006$ and 75.0% vs. 44.3%, $P < 0.001$, respectively). Patients who prescribed rehabilitation, except those in a serious condition due to complications, received rehabilitation.

### Operative findings and postoperative course

There was no difference in intraoperative findings between the two groups, except for the PV resection rate (Table 3). The morbidity rates categorized according to the Clavien-Dindo classification, CR-POPF, and pneumonia were not different between the two groups

**Table 1** Comparison of patients' characteristics between Octogenarians and Non-octogenarians

| Variable | Octogenarians ($n=44$) | | Non-octogenarians ($n=207$) | | *P* |
|---|---|---|---|---|---|
| Patient factor | | | | | |
| Male | 31 | (70.5) | 119 | (57.5) | 0.111 |
| Age (years) | 83 | (80–88) | 69 | (27–79) | < 0.001 |
| ASA ≥ 3 | 7 | (15.9) | 18 | (8.7) | 0.166 |
| BMI (kg/m$^2$) | 21.7 | (14.9–27.5) | 22.0 | (13.3–43.6) | 0.724 |
| Diagnosis | | | | | |
| Pancreatic cancer | 19 | (43.2) | 136 | (65.7) | < 0.001 |
| Cholangiocarcinoma | 19 | (43.2) | 25 | (12.1) | |
| Ampullary cancer | 4 | (9.1) | 15 | (7.3) | |
| Duodenum Cancer | 1 | (2.3) | 6 | (2.9) | |
| IPMN | 0 | (0) | 6 | (2.9) | |
| Neuroendocrine tumor | 0 | (0) | 6 | (2.9) | |
| Others | 1 | (2.3) | 13 | (6.3) | |
| Comorbidity | | | | | |
| Diabetes mellitus | 14 | (31.8) | 62 | (30.0) | 0.807 |
| Hypertension | 27 | (61.4) | 67 | (32.4) | < 0.001 |
| Hyperlipidemia | 9 | (20.5) | 34 | (16.4) | 0.660 |
| Coronary artery disease | 7 | (15.9) | 18 | (8.7) | 0.166 |
| Congestive heart failure | 0 | (0) | 1 | (0.5) | 1.000 |
| COPD | 0 | (0) | 4 | (1.9) | 1.000 |
| Cerebrovascular accident | 7 | (15.9) | 8 | (3.8) | 0.007 |
| Hemodialysis | 0 | (0) | 1 | (0.5) | 1.000 |
| Dementia | 2 | (4.5) | 3 | (1.4) | 0.212 |
| Depression | 2 | (4.5) | 2 | (1.0) | 0.070 |
| Antithrombogenic drug use | 13 | (29.5) | 30 | (14.5) | 0.016 |
| Long term steroid use | 2 | (4.5) | 3 | (1.4) | 0.212 |
| Preoperative biliary drainage | 35 | (79.5) | 88 | (42.5) | < 0.001 |
| Smoking habit | 2 | (4.5) | 32 | (15.5) | 0.055 |
| Preoperative treatment | | | | | |
| Chemotherapy | 9 | (20.5) | 9 | (44.4) | 0.004 |
| Chemoradiation | 1 | (2.3) | 2 | (1.0) | 0.441 |

Values are number (percentage) or median (range)

*ASA* American Society of Anesthesiologists physical status, *BMI* body mass index, *IPMN* intraductal papillary mucinous neoplasm, *COPD* chronic obstructive pulmonary disease

(Table 3). The LOS, LOFR, and 90-day mortality rates were also not different between the two groups. Among the elements of functional recovery days, octogenarians had a longer time to restore mobility to an independent level ($P<0.001$), while they had a shorter time to obtain adequate pain control ($P=0.040$) compared to non-octogenarians (Table 4). An additional analysis showed that the time to restore mobility to an independent level was not different between patients with or without sarcopenia (7.5 days vs. 8 days, $P=0.196$).

### Risk analysis for major complications

Univariate analysis identified male sex, BMI > 25 (kg/m$^2$), diagnosis of non-pancreatic cancer, diabetes mellitus, hypertension, preoperative chemotherapy, soft pancreas, bleeding, PV resection and PPPD as factors associated with major complications (Table 5). In the multivariate analysis, male sex, non-pancreatic cancer, sarcopenia, diabetes mellitus, hypertension, and long-term steroid use were determined as significant independent risk factors for major complications (Table 6).

Furthermore, we analyzed the odds ratio of sarcopenia as a major complication among patients aged > 80 years or < 80 years. The odds ratio in patients aged > 80 and < 80 were 6.50 (95% CI: 1.47–28.7, $P<0.001$) and 1.12 (95% CI: 0.49–2.60, $P=0.786$), respectively.

## Discussion

In this study, octogenarians had a higher rate of comorbidities, sarcopenia, and more impaired preoperative nutritional status than non-octogenarians and had a longer time to restore their ADLs after PD, even though nearly 90% of them received individualized rehabilitation under our ERAS protocol. However, their complication rate, LOS, and LOFR after PD were not different with those in non-octogenarians. In the multivariate analysis, age ≥ 80 years was not determined as a risk factor for major complications, whereas sarcopenia was determined as the risk factor.

The feasibility of PD in patients aged ≥ 80 years has been evaluated in several studies with small sample sizes [4, 6, 29]. Some systematic reviews have been conducted to address the shortage of this population in single centers, and the morbidity and mortality rates in octogenarians have been reported to be 27–58% and 0–11%, respectively [12–14]. Although these high morbidity and mortality rates indicate the importance of postoperative intensive care for patients aged ≥ 80 years, the impact of postoperative rehabilitation on postoperative outcomes in octogenarians has not been evaluated in previous studies, including these reviews [12–14, 17]. The main reason for this lack of evidence is the small number of octogenarians undergoing PD in Western countries. However, considering the growing number of elderly people worldwide, we need clear evidence regarding postoperative rehabilitation in this population. In this study, the proportion of patients aged ≥ 80 years was 18%, which was higher than that in previous studies, reflecting the aging society in Japan [29, 30]. Our findings would provide a

**Table 2** Comparison of rehabilitation, laboratory investigation, nutrition status and sarcopenia between Octogenarians and Non-octogenarian

| Variable | Octogenarians ($n=44$) | | Non-octogenarians ($n=207$) | | *P* |
|---|---|---|---|---|---|
| Preoperative laboratory data | | | | | |
| Hemoglobin (g/dL) | 11.5 | (8.6–14.8) | 12.4 | (8.2–16.9) | 0.010 |
| Total lymphocyte count (/mm3) | 1478 | (545–3381) | 1460 | (426–4558) | 0.497 |
| Platelet count ($\times 10^4$/mm3) | 20.3 | (9.7–38.7) | 23.0 | (8.9–59.9) | 0.049 |
| Bilirubin (umol/L) | 0.71 | (0.16–14.08) | 0.64 | (0.25–7.02) | 0.325 |
| Albumin (g/L) | 3.6 | (2.6–4.5) | 3.9 | (2.7–4.8) | < 0.001 |
| Creatinine (mg/dL) | 0.72 | (0.36–1.46) | 0.68 | (0.35–18.6) | 0.072 |
| T-chol (mg/dL) | 173 | (86–374) | 185 | (82–432) | 0.077 |
| HbA1c (%) | 6 | (4–11) | 6 | (4.7–11.7) | 0.955 |
| Nutrition status | | | | | |
| PNI | 43.6 | (31.8–54.3) | 46.0 | (32.8–62.7) | 0.005 |
| GPS (0/1/2) | 18/19/7 | | 151/40/16 | | < 0.001 |
| CONUT score | 18/17/7/0 | | 91/84/17/0 | | 0.318 |
| MNA-SF (Malnourished/At risk of malnutrition/ well-nourished) | 5/27/12 | | 15/83/109 | | 0.009 |
| NRS2002 ≥ 3 | 21 | (47.7) | 42 | (20.3) | < 0.001 |
| Sarcopenia | 14 | (31.8) | 34 | (16.4) | 0.018 |
| Postoperative rehabilitation | 38 | (86.4) | 91 | (44.0) | < 0.001 |
| Perioperative rehabilitation | 7 | (15.9) | 10 | (4.8) | 0.016 |

Values are number (percentage) or median (range)]

*PNI* prognostic nutritional index, *GPS* Glasgow Prognostic Score, *CONUT* Controlling Nutritional Status, *MNA-SF* Mini Nutritional Assessment-Short Form, *NRS* Nutritional Risk Screening

**Table 3** Comparison of patients' intraoperative findings between Octogenarians and Non-octogenarians

| Variable | Octogenarians ($n=44$) | | Non-octogenarians ($n=207$) | | *P* |
|---|---|---|---|---|---|
| Soft pancreas | 20 | (45.5) | 92 | (44.4) | 0.327 |
| MPD ≤ 3 mm | 16 | (41.7) | 87 | (48.9) | 0.384 |
| Operation time (min) | 486 | (338–903) | 503 | (246–989) | 0.518 |
| Bleeding (ml) | 254 | (30–745) | 240 | (15–1470) | 0.882 |
| PV resection | 9 | (20.5) | 84 | (40.6) | 0.012 |
| PPPD (yes) | 8 | (18.2) | 48 | (23.2) | 0.818 |

Values are number (percentage) or median (range)

*MPD* main pancreatic duct, *PV* portal vein, *PPPD* pylorus-preserving pancreatoduodenectomy

better understanding of patients aged ≥ 80 years not only to Japan but also to countries with a growing number of elderly people.

In our study, age ≥ 80 years was not determined as a risk factor for major morbidity, which was the same as a previous meta-analysis performed by Kim [14]. While, sarcopenia was determined as the risk factor, even though patients with sarcopenia received individualized rehabilitation. Our findings conflicted with those of a meta-analysis performed by Ratnayake et al. that rarely included patients aged ≥ 80 years, whereas Wagner et al. similarly determined sarcopenia as a risk factor for postoperative morbidity in a population that included patients aged ≥ 80 years [15, 31]. The different findings of previous studies and our study suggest that the disadvantage of sarcopenia could be profound among elderly patients. The profound disadvantage of sarcopenia could be explained by the higher burden of comorbidities in elderly patients than that in younger patients. In our analysis, sarcopenia was associated with major complications in patients aged ≥ 80 years who had a higher rate of comorbidities but not in those aged < 80 years, which supports our hypothesis. Moreover, in our study, postoperative rehabilitation was not identified as a favorable factor for major morbidity, suggesting another strategy to overcome the disadvantages of sarcopenia. Recently, Barberan-Garcia et al. reported that preoperative rehabilitation in high-risk patients undergoing major digestive surgery decreased the number of morbidities in a randomized controlled study, which encouraged us to deliver preoperative rehabilitation to patients with sarcopenia [32].

**Table 4** Comparison of postoperative findings between Octogenarians and Non-octogenarians

| Variable | Octogenarians (*n* = 44) | | Non-octogenarians (*n* = 207) | | *P* |
|---|---|---|---|---|---|
| Morbidity | | | | | |
| Clavien-Dindo ≥ II | 31 | (70.5) | 132 | (63.8) | 0.399 |
| Clavien-Dindo ≥ IIIa (major complication) | 11 | (25.0) | 51 | (24.6) | 0.960 |
| Clavien-Dindo ≥ IV | 4 | (9.1) | 8 | (3.9) | 0.233 |
| Clinically relevant POPF | 13 | (29.5) | 59 | (28.5) | 0.805 |
| DGE | 10 | (22.7) | 43 | (20.8) | 0.773 |
| Bile leakage | 2 | (4.5) | 3 | (1.4) | 0.212 |
| Postoperative Hemorrhage | 2 | (4.5) | 6 | (2.9) | 0.632 |
| SSI | 5 | (11.4) | 21 | (10.1) | 0.787 |
| Pneumonia | 2 | (4.5) | 5 | (2.4) | 0.355 |
| Reoperation | 4 | (9.1) | 5 | (2.4) | 0.053 |
| Length of hospital stay (days) | 31 | (12–163) | 28 | (11–138) | 0.435 |
| Length of functional recovery (days) | 19 | (6–80) | 15 | (5–76) | 0.110 |
| Adequate pain control | 5 | (3–14) | 6 | (2–53) | 0.040 |
| Restoration of mobility to an independent level | 14 | (5–63) | 8 | (2–76) | < 0.001 |
| Ability to maintain sufficient caloric intake | 17 | (5–80) | 13 | (3–66) | 0.451 |
| No signs of active abdominal infection | 6 | (2–55) | 5 | (2–73) | 0.460 |
| 90-day mortality | 0 | (0) | 5 | (2.4) | 1.000 |
| Failure to rescue | 0 | (0) | 5/51 | (9.8) | 0.575 |

Values are number (percentage) or median (range)

*POPF* postoperative pancreatic fistula, *DGE* delayed gastric emptying, *SSI* surgical site infection

Unfortunately, postoperative rehabilitation was not an independent favorable factor for major morbidities. However, it could have contributed to a decrease in the postoperative pneumonia rate because our rehabilitation program consisted mainly of aerobic exercises that stimulated the inspiratory muscle. Postoperative pneumonia was identified as the second most common non-operative morbidity after pancreatic resection [33]. Nagle et al. reported that 55% of postoperative pneumonia cases developed Clavien-Dindo grade IV or V, and which was associated with a very high 90-day mortality rate of 30% after PD [34]. Therefore, the prevention of postoperative pneumonia is key to decreasing major morbidity after PD, and there is promising evidence in literature that a multimodal prehabilitation may be instrumental in decreasing post-operative pulmonary complications following pancreatic surgery [35]. Although the positive effect of rehabilitation on the prevention of postoperative pneumonia has been reported in many previous studies, its effect in octogenarians requires further evaluation because the postoperative pneumonia rate in octogenarians is higher than that in non-octogenarian [29, 36–43]. Although pulmonary function decreases with age, the postoperative pneumonia rates in octogenarians and non-octogenarians were not different under our rehabilitation-enhanced ERAS protocol, which could provide new evidence that encourages postoperative rehabilitation in high-risk patients.

Another interesting result of our study was that the time to restore mobility did not influence the LOFR or LOS in patients aged ≥ 80 years. Because there are few rehabilitation or nursing facilities and most patients are discharged to their homes after full recovery in Japan, we could collect detailed data about the patients' recovery process. Activities of daily living in the elderly decline easily, and they require a long time to improve once it declines. In fact, the time to restore mobility to an independent level was longer in octogenarians than in non-octogenarians in our study; however, the effect on LOS and LOFR was stronger for the recovery of dietary intake than for the restoration of mobility in the octogenarian group under the rehabilitation-enhanced ERAS protocol. Although early and scheduled mobilization after PD is recommended, there is little evidence, including that for other types of abdominal surgery [17]. In addition, early and adequate mobilization following pancreatoduodenectomy was perceived to be one of the most challenging components to achieve in a recent survey [44]. A recent randomized controlled study from Canada showed that the time from surgery until the achievement of standardized hospital discharge criteria did not decrease by staff-directed facilitation of early mobilization in

**Table 5** Univariate analysis of risk factors of major complications

| Variable | Major complication ($n=62$) | | Minor or no complication ($n=189$) | | *P* |
|---|---|---|---|---|---|
| Patient factor | | | | | |
| Male | 49 | (79) | 101 | (53.4) | < 0.001 |
| Age ≥ 80 (years) | 11 | (17.7) | 33 | (17.5) | 0.960 |
| ASA ≥ 3 | 8 | (12.9) | 17 | (9) | 0.373 |
| BMI > 25 (kg/m$^2$) | 18 | (29) | 25 | (13.2) | 0.004 |
| Diagnosis | | | | | |
| Pancreatic cancer | 29 | (46.8) | 126 | (66.7) | < 0.001 |
| Comorbidity | | | | | |
| Diabetes mellitus | 26 | (41.9) | 50 | (26.5) | 0.021 |
| Hypertension | 33 | (53.2) | 61 | (32.3) | 0.003 |
| Hyperlipidemia | 13 | (21) | 30 | (15.9) | 0.356 |
| Coronary artery disease | 9 | (14.5) | 16 | (8.5) | 0.220 |
| Congestive heart failure | 0 | (0) | 1 | (0.5) | 1.000 |
| COPD | 1 | (1.6) | 3 | (1.6) | 1.000 |
| Cerebrovascular accident | 3 | (4.8) | 12 | (6.3) | 1.000 |
| Hemodialysis | 0 | (0) | 1 | (0.5) | 1.000 |
| Antithrombogenic drug | 13 | (21) | 30 | (15.9) | 0.356 |
| Dementia | 3 | (4.8) | 2 | (1.1) | 0.098 |
| Depression | 0 | (0) | 4 | (2.1) | 0.248 |
| Long-term steroid use | 3 | (4.8) | 2 | (1.1) | 0.098 |
| Preoperative biliary drainage | 28 | (45.2) | 95 | (50.3) | 0.485 |
| Smoking habit | 9 | (14.5) | 25 | (13.2) | 0.797 |
| Preoperative treatment | | | | | |
| Chemotherapy | 17 | (32.7) | 81 | (50) | 0.040 |
| Chemoradiation | 1 | (1.6) | 2 | (1.1) | 0.575 |
| Preoperative laboratory data | | | | | |
| Hemoglobin (male < 13.5 g/dL, female < 11.4 g/dL) | 17 | (27.4) | 64 | (33.9) | 0.346 |
| Total lymphocyte count < 2000/mm3 | 54 | (87.1) | 151 | (79.9) | 0.203 |
| Platelet count < $15 \times 10^4$/mm3 | 8 | (12.9) | 14 | (7.4) | 0.184 |
| Bilirubin ≥ 2.0 umol/L | 2 | (3.2) | 18 | (9.5) | 0.174 |
| Albumin < 3.0 g/L | 7 | (5) | 104 | (55) | 0.473 |
| Creatinine ≥ 1.5 mg/dL | 1 | (1.6) | 4 | (2.1) | 1.000 |
| T-chol ≥ 200 mg/dL | 23 | (28.3) | 58 | (33.3) | 0.483 |
| HbA1c ≥ 7.0% | 15 | (24.6) | 29 | (15.9) | 0.129 |
| Nutrition status | | | | | |
| PNI ≤ 340 | 11 | (17.7) | 31 | (36.4) | 0.806 |
| GPS (0/1/2) | 38/20/4 | | 131/59/4 | | 0.150 |
| CONUT score | 28/25/7/0 | | 81/76/17/0 | | 0.906 |
| MNA-SF (Malnourished/At risk of malnutrition/well-nourished) | 3/24/35 | | 17/86/86 | | 0.264 |
| NRS2002 ≥ 3 | 17 | (27.4) | 46 | (24.3) | 0.892 |
| Sarcopenia | 16 | (25.8) | 32 | (16.9) | 0.123 |
| Postoperative rehabilitation | 38 | (61.3) | 91 | (48.1) | 0.072 |
| Perioperative rehabilitation | 4 | (6.5) | 13 | (6.5) | 1.000 |
| Operative findings | | | | | |
| Soft pancreas | 38 | (61.3) | 74 | (39.2) | 0.006 |
| MPD ≤ 3 mm | 29 | (52.7) | 74 | (45.7) | 0.366 |
| Operation time > 600 min | 16 | (25.8) | 34 | (18.0) | 0.181 |
| Bleeding > 500 ml | 13 | (21.0) | 21 | (11.1) | 0.049 |
| PV resection | 16 | (25.8) | 77 | (40.7) | 0.035 |
| PPPD (yes) | 21 | (33.9) | 35 | (18.5) | 0.012 |

Values are number (percentage) or median (range)

*ASA* American Society of Anesthesiologists physical status, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *PNI* prognostic nutritional index, *GPS* Glasgow Prognostic Score, *CONUT* Controlling Nutritional Status, *MNA-SF* Mini Nutritional Assessment-Short Form, *NRS* Nutritional Risk Screening, *MPD* main pancreatic duct, *PV* portal vein, *PPPD* pylorus-preserving pancreatoduodenectomy

**Table 6** Multivariate analysis of risk factors for major complications

| Variable | Odds ratio (95% CI) | *P* |
|---|---|---|
| Male | 2.591 (1.190–5.638) | 0.016 |
| Age ≥ 80 | 0.448 (0.177–1.133) | 0.090 |
| BMI > 25 (kg/m$^2$) | 2.197 (0.969–4.983) | 0.060 |
| Pancreatic cancer | 0.396 (0.188–0.835) | 0.015 |
| Diabetes mellitus | 2.263 (1.065–4.806) | 0.034 |
| Hypertension | 2.150 (1.082–4.272) | 0.029 |
| Long-term steroid use | 16.131 (1.983–131.2) | 0.009 |
| Sarcopenia | 2.459 (1.061–5.699) | 0.036 |
| Postoperative rehabilitation | 1.175 (0.577–2.391) | 0.656 |
| Soft pancreas | 1.930 (0.925–4.025) | 0.008 |

*BMI* body mass index

patients who underwent colorectal surgery [45]. However, this study included patients aged < 75 years, with or without sarcopenia, and 80% of the patients underwent laparoscopic surgery. In contrast, a report from a Japanese high-volume center that included patients aged 90 years undergoing PD showed that LOS was significantly shorter in patients who received perioperative rehabilitation than in those who did not [39]. These varying findings, including ours, imply that rehabilitation could be beneficial in older patients or after more invasive surgical procedures. Further studies are required to draw definitive conclusions regarding the effects of rehabilitation after surgery.

This study has some limitations. First, this study has a nature of retrospective study. The indication for rehabilitation depends on surgeons rather than the objective method. Second, the relatively small sample size of octogenarians in this study might have affected the statistical outcomes, although the proportion of octogenarians in our study was 18%, reflecting an aging society in Japan. In further study, a nationwide study would be required. Third, the long LOS under our meticulous postoperative management for POPF and the unique Japanese medical environment with a shortage of rehabilitation or nursing facilities could mitigate the difference in LOS between octogenarians and non-octogenarians. Therefore, we used the time to functional recovery to evaluate the efficacy of rehabilitation because LOFR has been reported to be a more objective outcome measure than LOS that is frequently influenced by external factors. Fourth, the effect of preoperative rehabilitation was not evaluated because preoperative rehabilitation was offered only for patients who were admitted a week before surgery for glycemic control, and the indication depended on the surgeon. In this study, less than 7% of our patients received it; therefore, the effect of the statistical results would be minimal. Lastly, some factors in patients' background and surgical procedures, such as the proportion of pancreatic ductal adenocarcinoma and portal vein resection, were different between octogenarians and non-octogenarians, which could affect the postoperative major complications.

In conclusion, the postoperative major complication rate, LOS, and LOFR after PD in octogenarians under the rehabilitation-enhanced ERAS protocol were comparable to those in non-octogenarians. Our patient population that included many patients aged ≥ 80 years with many comorbidities would be that of other countries in the future. Our findings would make it possible to prepare for better surgical management of older surgical candidates.

**Abbreviations**

| | |
|---|---|
| PD | Pancreaticoduodenectomy |
| ERAS | Enhanced recovery after surgery |
| LOS | Length of hospital stay |
| LOFR | Length of functional recovery |
| SMA | Skeletal muscle area |
| SMI | Skeletal muscle index |
| SSPPD | Subtotal stomach-preserving pancreaticoduodenectomy |
| PPPD | Pylorus-preserving pancreaticoduodenectomy |
| ASA | Anesthesiologists physical status |
| PNI | Prognostic nutritional index |
| CONUT | Controlling nutritional status score |
| GPS | Glasgow prognostic score |
| NRS2002 | Nutrition risk screening tool |
| MNA-SF | Mini Nutritional Assessment Short Form |
| POPF | Postoperative pancreatic fistula |
| ISGPS | International Study Group of Pancreatic Surgery |
| DGE | Delayed gastric emptying |

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**Patients consent statement**
The requirement for informed consent was waived owing to the retrospective study design.

**Clinical trial registration**
Not applicable.

**Declaration of generative AI and AI-assisted technologies in the writing process**
During the preparation of this work, the authors used Paperpal in order to improve readability and language. After using this tool, the authors reviewed and edited the content as need and take full responsibility for the content of the publication.

**Authors' contributions**
Study conception and design: N.I, Y.T, R.Y, Y.M, H.S, A.S; Acquisition of data: N.I; Analysis and interpretation of data: N.I, Y.T, A.S; Drafting of manuscript: N.I; Critical revision of manuscript: Y.T, A.S

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**Data availability**
The data that support the findings of this study are not publicly available due to the privacy of research participants but are available from the corresponding author Akio Saiura on reasonable request. No funding was received for conducting this study.

## Declarations

**Ethics approval and consent to participate**
This study has been approved by the appropriate ethics committee, with reference number E23-0315-N01. Therefore, it has been conducted in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki and its subsequent amendments. Informed consent was obtained through an opt-out process on the Juntendo University Hospital website.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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## Publisher's Note