

Long-term impact of acute pancreatitis on patients' quality of life: A multi-center prospective study in Japan

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Research in context

Evidence before this study: We searched PubMed for English-language articles published until April 2025 using the keywords “acute pancreatitis” and “quality of life.” Previous studies indicated that acute pancreatitis adversely affects health-related quality of life (HRQoL), particularly in the physical domain. However, most of these studies focused on patients with severe acute pancreatitis. In addition, few studies have evaluated longitudinal changes in HRQoL or its impact on social outcomes (e.g., return to work), especially in Asian healthcare settings.

Added value of this study: This is the first prospective, multi-center cohort study that was conducted in Japan and comprehensively examines longitudinal changes in HRQoL and return-to-work status after acute pancreatitis across a full spectrum of disease severity. By evaluating HRQoL (using SF-12) and return-to-work outcomes at 3 and 12 months post-onset, and applying causal inference methods, we demonstrate that incomplete return to work is common even among patients with a mild disease. This study identifies both early and late-phase determinants, including initial disease severity, female sex, and reduced subjective HRQoL, underscoring the multifactorial nature of long-term social recovery.

Implications of all the available evidence: Our results reveal that in the universal healthcare system of Japan, ensuring equal access to acute and follow-up care, approximately 20 % of the patients with acute pancreatitis experience incomplete return to work even one year after onset, suggesting a gap in current recovery support strategies. A two-phase recovery approach might thus be necessary: early interventions addressing physical function and nutrition, and later-stage interventions supporting psychosocial and occupational reintegration. These findings are particularly relevant for aging societies and other Asia-Pacific health systems facing similar challenges in balancing clinical and social recovery. Policymakers and clinicians should prioritize long-term, patient-centered support beyond the acute care phase.

Abstract

Background: While acute pancreatitis often resolves, its long-term impact on health-related quality of life (HRQoL) and return to work remains unclear. This study investigated the longitudinal changes in HRQoL and factors affecting incomplete return to work following acute pancreatitis.

Methods: This multi-center, prospective cohort study included patients aged ≥ 18 years hospitalized with acute pancreatitis across 20 hospitals in Japan and was conducted from April 2018 to March 2024. Patients were consecutively enrolled and completed baseline and follow-up HRQoL assessments at 3 and 12 months. The severity of acute pancreatitis, demographic factors, and HRQoL parameters, including physical component score (PCS) assessed with the 12-item Short-Form Health Survey version 2 and return-to-work status, were evaluated.

Findings: Among 284 enrolled patients, 226 were included in the primary endpoint analysis. At 3 months, incomplete return to work occurred in 49 (21.7%) patients, who more frequently exhibited a PCS ≤ 45 than did those with complete return to work (73.5% vs. 24.9%). Logistic regression and causal analyses indicated that female sex, high admission APACHE II score on admission, and reduced subjective (self-reported) HRQoL were associated with incomplete return to work at 3 months. At 12 months, incomplete return to work occurred in 17.5% of patients. Factors influencing return-to-work status differed structurally between 3 and 12 months.

Interpretation: Approximately 20% of patients with acute pancreatitis had incomplete return to work at 3 and 12 months. At 3 months, this was associated with lower PCS and caused by female sex, initial disease severity, and poor subjective HRQoL.

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Keywords: Acute pancreatitis; quality of life; physical functional performance; return to work; long-term impact

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Introduction

Acute pancreatitis is a common disease that often requires hospitalization, affecting 34 per 100,000 people annually worldwide.¹ While most cases resolve within a week,² approximately 20% of them become severe, with a mortality rate of 20–40%.^{3,4} Advances in treatment⁵ have significantly improved patient survival rates.^{6,7} In Japan, nationwide efforts to standardize care (e.g., evidence-based guideline dissemination and early severity scoring system implementation) have contributed to a marked reduction in mortality, from 15.1 % in the 1980s to only 1.8 % in recent years.⁶ As a result, clinical focus has shifted from acute management toward long-term outcomes, including physical recovery, health-related quality of life (HRQoL), and social reintegration. Patients are expected to return to work after recovery, given that the disease mainly affects the productive generation aged 50–60 years.^{6,8} However, several patients might continue to face persistent problems related to physical functioning and social participation despite the clinical resolution of the disease.

Several studies have examined the HRQoL after acute pancreatitis, with a recent review emphasizing its negative impact on HRQoL in severe cases.⁹ However, research on mild and moderate cases remains limited, and the long-term effects of disease severity on HRQoL are poorly understood. Moreover, few studies have explored the social and occupational consequences of acute pancreatitis, such as delayed return to work, particularly in East Asian healthcare settings, where social structures and employment patterns might differ from those of Western contexts.

To address this, we conducted the LONG-term impact of acute pancreatitis on patients' quality of life (LONG-TONE) study, a multi-center prospective questionnaire study in Japan. Using multivariate and causal analyses, we examined the changes in HRQoL and factors that inhibit recovery after acute pancreatitis.

Methods

Study design

This multi-center prospective observational study was conducted at 20 institutions in Japan from April 2018 to March 2024 to assess changes in HRQoL in patients with acute pancreatitis using questionnaires at admission and at 3 and 12 months post-onset. The study was approved by the Kurashiki Central Hospital Ethics Committee (number: 2833) and complied with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Inclusion and exclusion criteria

The inclusion criteria were as follows: i) a diagnosis of acute pancreatitis based on the revised Atlanta criteria,¹⁰ ii) admission to the participating institutions, iii) age \geq 18 years, and iv) provided written informed consent for study participation. The exclusion criteria included i) history of chronic pancreatitis, ii) treatment for \geq 24 h at another institution before admission, iii) new-onset acute pancreatitis during hospitalization, iv) inability to complete the questionnaire appropriately, v) alcohol dependence as defined by the World Health Organization,^{11,12} vi) pre-existing mental disorders requiring professional treatment, g) pre-existing severe organ failure or immunocompromised status as determined by the acute physiologic assessment and chronic health evaluation II (APACHE II) scoring system,¹³ and h) any other conditions deemed inappropriate for study participation.

Data collection and follow-up

The characteristics of the patients, including age, sex, body mass index, etiology of acute pancreatitis, and baseline HRQoL scores (Short-Form 12 version 2 [SF-12v2] scores¹⁴), were collected on admission. Vital signs (body temperature, blood pressure, pulse, and respiratory

rate) and laboratory data on admission were used to evaluate the severity of acute pancreatitis (Table S1). Pre-existing comorbidities were assessed using the Charlson comorbidity index (CCI).¹⁵ The severity of acute pancreatitis was evaluated according to the revised Atlanta criteria,¹⁰ Japanese (JPN) severity criteria and prognostic factors,¹⁶ APACHE II scores,¹³ and disseminated intravascular coagulation (DIC) scores. Diagnoses of local complications, such as acute necrotic collection (ANC), walled-off necrosis (WON), and pancreatic pseudocyst (PPC), were made based on clinical and imaging findings in accordance with the revised Atlanta criteria.¹⁰ Treatment was performed following the guideline recommendations.¹⁶ Expert physicians in abdominal emergencies or gastroenterology recorded treatment data at discharge, including hospitalization length, use of intensive care unit (ICU), mechanical ventilation, endoscopic retrograde cholangiopancreatography, enteral nutrition, time to oral feeding, interventions for local complications, and total in-hospital costs.

HRQoL assessment

Patients' HRQoL was assessed using the SF-12v2 and return-to-work status at baseline, 3 months, and 12 months after acute pancreatitis onset. Baseline HRQoL was assessed at admission based on patient recall, while expert physicians prospectively conducted follow-ups at 3 and 12 months, either in the hospital or by telephone.

The SF-12v2 is a widely used self-administered questionnaire that evaluates HRQoL across 12 items spanning eight domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). These domains are summarized into three component scores: physical component score (PCS), mental component score (MCS), and role-social component score (RCS). Based on the general Japanese population, each score was standardized to a mean of 50 and a standard deviation (SD) of 10.

Return-to-work status was classified as “complete return,” “partial return,” or “non-return.” Subjective HRQoL (self-reported HRQoL change) at 3 and 12 months was assessed by comparing post-onset status to baseline, with four response options: “improved,” “unchanged,” “slightly worsened,” and “worsened.” For analysis, “improved” and “unchanged” were grouped as “maintained/improved,” and the others as “worsened.”

Study endpoints

The primary endpoint of this study was to assess the social impact of acute pancreatitis on HRQoL 3 months after onset. To investigate this, we compared the changes in PCS at 3 months from the onset between patients with and without complete return to work. Those who answered “partial return” or “non-return” were classified into the incomplete return to work group. The secondary endpoints included the differences in MCS, RCS, and subjective HRQoL at 3 and 12 months, as well as PCS at 12 months between patients with and without complete return to work.

Sample size analysis

To calculate the sample size, we first assumed that at least 15% of patients with acute pancreatitis would experience incomplete return to work 3 months after disease onset, based on data from other diseases.^{17,18} The proportions of patients with a PCS < 45 among those with complete and incomplete return to work were assumed to be 40% and 75%, respectively, with an SD of 10. To detect a statistically significant difference in PCS between these groups at an alpha level of 0.05 and a power of 0.9, the total sample size calculated using the chi-squared test with Yates’ correction was estimated to be at least 212 patients.

Two protocol amendments were made to maintain statistical power: in July 2019, the target sample size was increased from 200 to 300, and in November 2020, the study period

was extended to March 2024. As the number of dropouts was lower than expected, and over 212 patients completed the 3-month follow-up visits, enrollment was closed in December 2023 with a total of 284 participants.

Statistical analysis

Parametric continuous variables are shown as mean \pm SD and compared using Student t-test; non-parametric variables are shown as median [interquartile range] and compared using the Mann–Whitney U test. Changes in HRQoL were assessed using a paired t-test. Categorical variables, expressed as numbers (percentages), were compared using the Fisher exact test; trends were evaluated using the Cochran–Armitage test. Binomial logistic regression was used to adjust for confounders. Variables with a variance inflation factor > 10 were excluded to address multicollinearity. Two-tailed $p < 0.05$ was considered significant. Analyses were conducted using SPSS version 27.0¹⁹ (IBM Corp., Armonk, NY, USA), R version 4.1.2²⁰ (The R Foundation for Statistical Computing, Vienna, Austria), and EZR²¹ (Saitama Medical Center, Japan), a graphical interface for R.

Causal analysis

Logistic regression identifies statistical associations but does not determine causal relationships between explanatory and outcome variables. To clarify the direction of causality, we applied the DirectLiNGAM (Linear Non-Gaussian Acyclic model) algorithm.²² Model fit was assessed using the goodness of fit index (GFI) and adjusted GFI (AGFI), with values near 1 indicating a good fit, and the reliability of causal analysis was confirmed via 100 bootstrap resamples to calculate bootstrap probabilities.²³ Among the factors associated with incomplete return to work in the logistic regression analysis ($p < 0.10$), those with a bootstrap probability of ≥ 0.95 in the LiNGAM analysis were considered definite

causes/consequences of incomplete return, while those with a bootstrap probability between 0.50 and 0.94 were considered probable causes/consequences. Causal and bootstrap analyses were performed using the Causalas software (SCREEN Advanced System Solutions, Japan).

Results

Characteristics of patients with complete and incomplete return to work at 3 months post-onset

A total of 284 patients were enrolled from 16 of 20 institutions, with 226 (79.6%) completing the 3-month follow-up (Figure 1A). Among them, 149 (65.9%) were male, with a median age of 67 years (Table 1). Etiologies of pancreatitis included gallstones (73, 32.3%), idiopathic causes (56, 24.8%), alcohol consumption of ≥ 40 g/day (35, 15.5%), and others (62, 27.4%). Mean baseline PCS, MCS, and RCS scores were 45.8, 56.8, and 49.9, respectively. The baseline PCS was almost aligned with the Japanese average values when adjusted for age (Figure S1). Based on the revised Atlanta criteria, 178 (78.8%), 31 (13.7%), and 17 (7.5%) patients had mild, moderately severe, and severe acute pancreatitis, respectively; JPN criteria identified 138 (61.1%) and 88 (38.9%) mild and severe cases, respectively. Thirty-six (15.9%) patients experienced local complications: 26, one, four, four, and one had sterile ANC, infected ANC, sterile WON, infected WON, and sterile PPC, respectively. In this 3-month cohort, the median hospital stay was 10 days. Nine (4.0%) and five (2.2%) patients required ICU care and mechanical ventilation, respectively; moreover, four (1.8%) underwent drainage procedures for local complications. The median in-hospital cost was ¥577,036 (approximately USD 6,079 at 2022 rates).

Significant differences were observed between patients with complete return to work ($n = 177$) and those without ($n = 49$) regarding several factors: baseline PCS (47.2 ± 11.5 vs. 40.9 ± 12.0 , $p < 0.01$), RCS (51.0 ± 9.4 vs. 46.1 ± 11.9 , $p < 0.01$), revised Atlanta severity

classification on admission (mild/moderate/severe: 146/20/11 vs. 32/11/6, $p = 0.01$), APACHE II score (6 vs. 8 [median], $p < 0.01$), DIC development (1.1% vs. 12.2%, $p < 0.01$), and infected WON (0.6% vs. 6.1%, $p = 0.03$) (Table 1). Compared with patients with complete return to work, those with incomplete return at 3 months had longer hospital stays (9 vs. 12 days, $p < 0.01$), higher ICU admission rates (2.3% vs. 10.2%, $p = 0.04$), and more interventions for local complications (0.6% vs. 6.1%, $p = 0.05$). Their median in-hospital cost was also higher (543,360 vs. 660,962 yen, $p < 0.01$).

Comparison of HRQoL between patients with complete and incomplete return to work at 3 months after onset

At 3 months, mean PCS, MCS, and RCS were 45.9 ± 13.0 , 57.6 ± 8.3 , and 49.5 ± 9.8 , respectively. Score changes (baseline to 3 months) with 95% CI and p -values were as follows: PCS (+0.11, -1.48 to +1.70, $p = 0.89$), MCS (+0.80, -0.51 to +2.10, $p = 0.23$), and RCS (-0.45, -1.98 to +1.08, $p = 0.57$) (Figure 1B). No significant differences were seen in seven SF-12v2 domains (PF, RP, BP, VT, SF, RE, MH), whereas GH scores improved (51.7 ± 11.1 vs. 54.1 ± 10.0 , $p < 0.01$) (Figure 1C). Regarding return-to-work status, 78.3%, 15.9%, and 5.8% of patients reported complete return, partial return, and non-return, respectively (Figure 1D). Delta PCS, MCS, and RCS scores (between baseline and 3 months) were significantly lower in those with incomplete return to work than in patients with complete return to work: PCS ($+1.32 \pm 10.95$ vs. -4.28 ± 15.05 , $p < 0.01$), MCS ($+1.54 \pm 9.35$ vs. -1.88 ± 11.67 , $p = 0.03$), and RCS ($+0.68 \pm 10.86$ vs. -4.52 ± 13.60 , $p < 0.01$) (Figure 1E). When focusing on self-reported HRQoL assessments, of the 177 patients with maintained/improved subjective HRQoL at 3 months, only 15 (8.5%) experienced incomplete return to work, whereas 34 of 49 (69.4%) with worsened HRQoL did ($p < 0.01$) (Figure 1F). PCS-3M ≤ 45 was observed in

44/177 (24.9%) and 36/49 (73.5%) with complete and incomplete return, respectively ($p < 0.01$), aligning with the sample size assumptions.

Logistic regression and causal analysis

As shown in Figure 1D, 21.7% of patients experienced incomplete return to work at 3 months after onset. Given that these cases tended to be more severe and required intensive treatment (Table 1), we adjusted for potential confounding using binomial logistic regression to identify factors associated with incomplete return. The results (Table 2) showed that female sex, delta PCS-3M, delta RCS-3M, APACHE II score, and subjective HRQoL-3M were significantly associated ($p < 0.05$) or showed a trend toward association ($p < 0.10$) with incomplete return.

Model fit in the causal analysis was acceptable (GFI: 0.90, AGFI: 0.84). As shown in Figure 2 (red lines: bootstrap probability ≥ 0.95), worsened subjective HRQoL-3M was a definite cause of incomplete return to work; female sex and high APACHE II scores were probable causes. A decline in delta RCS-3M was a definite consequence. Causal effects (bootstrap probabilities) for incomplete return were subjective HRQoL-3M, 0.58 (1.00); female sex, 0.14 (0.57); APACHE II, 0.02 (0.85); and delta RCS-3M, -0.41 (1.00).

HRQoL of patients with incomplete return to work at 12 months post-onset

We performed the same series of analyses on the 12-month cohort ($n = 211$) as we did on the 3-month cohort. In this cohort, 174 (82.5%) and 37 (17.5%) reported complete and incomplete return (Figure 3A). The mean MCS was significantly higher than the baseline (Figure 3B, $p < 0.01$). Unlike in the 3-month cohort, severe cases requiring invasive treatments were not significantly more frequent among patients with incomplete return to work at 12 months (Table S2). Among the 211 patients, 69 (32.7%) and 29 (13.7%) were readmitted for any cause within a year and due to pancreatitis, respectively. Compared with

patients with complete return to work, those with incomplete return to work showed significant reductions in PCS and RCS at 12 months (delta PCS-12M, $+1.31 \pm 11.32$ vs. -3.08 ± 15.37 , $p < 0.05$; delta RCS-12M, $+0.70 \pm 10.96$ vs. -4.53 ± 15.24 , $p < 0.05$) (Figure 3C). Among the 174 patients with maintained/improved subjective HRQoL-12M, 160 (92%) experienced complete return to work, whereas only eight of the 37 (21.6%) with worsened HRQoL-12M did ($p < 0.01$) (Figure 3D). Binomial logistic regression identified several variables that were significantly or marginally associated with incomplete return to work. The odds ratios (95% CI, p -value) were as follows: age, 0.92 (0.86–0.98, $p < 0.01$); female sex, 3.29 (0.96–11.3, $p = 0.06$); delta MCS-12M, 0.92 (0.86–0.98, $p = 0.02$); CCI, 1.49 (0.96–2.34, $p = 0.08$); timing of oral feeding, 1.86 (0.91–3.78, $p = 0.09$); and subjective HRQoL-12M, 9.00 (8.18–103.00, $p < 0.01$) (Table S3).

However, in the causal analysis, none of them were identified as definite or probable causes of incomplete return to work at 12 months (Figure 3E). Worsened subjective HRQoL-12M and female sex were considered definite and probable consequences, respectively. The causal effects (bootstrap probabilities) were as follows: worsened subjective HRQoL-12M, 1.16 (1.00); and female sex, 0.30 (0.74).

Discussion

Among the patients with acute pancreatitis who completed follow-up at 3 months from the onset, 21.7% experienced incomplete return to work. Patients with incomplete return to work had higher severity, required more invasive care, and needed higher in-hospital costs. Logistic regression analysis revealed that incomplete return to work at 3 months, accompanied by significantly lower physical scores, was associated with five factors: female sex, delta PCS-3M, delta RCS-3M, APACHE II score, and subjective HRQoL-3M. At 12 months, six factors were identified: age, female sex, delta MCS-12M, CCI, timing of oral feeding, and subjective

HRQoL-12M. None of these factors were associated with initial disease severity or physical function, suggesting a shift in the determinants compared with those of the 3-month profile.

Causal analysis clarified these dynamics. At 3 months, APACHE II score, female sex, and reduced subjective HRQoL were upstream (parent) factors contributing to incomplete return to work. However, by 12 months, female sex and subjective HRQoL appeared as downstream (child) outcomes, suggesting that incomplete return to work itself may have negatively influenced HRQoL. This shift may reflect the different nature of factors affecting return to work over time. In the short term, physical sequelae, such as pancreatic exocrine dysfunction,²⁴ may have delayed recovery. By contrast, in the long term, social factors, such as employment type, might have played a greater role than physical factors in this shift at 12 months.

A possible explanation for the incomplete return to work observed over 12 months among women is high prevalence of part-time or non-regular employment among Japanese women,²⁵ a form of employment that may limit workplace support for reintegration after illness.²⁶ Such structural employment differences should be considered when interpreting long-term social outcomes, particularly in East Asian countries, where traditional gender roles and employment patterns differ from those in Western nations.²⁷ The fact that our cohort was drawn entirely from Japanese hospitals highlights the importance of considering regional social determinants of health in recovery from acute illnesses. Nonetheless, our findings underscore the need for early-phase interventions focused on physical recovery (e.g., nutritional counseling and rehabilitation) and later-phase strategies targeting psychosocial and occupational reintegration.

In this study, we initially estimated the incomplete return-to-work rate at 3 months to be 15%; however, the actual rate exceeded 20%. This rate is higher than that reported in patients with other acute diseases.^{28,29} Acute pancreatitis impairs the exocrine function of the

pancreas, which is strongly involved in the maintenance of skeletal muscles.²⁹ Given the high prevalence of PCS < 45 among patients with incomplete return at 3 months, exocrine dysfunction and subsequent loss of muscle mass may have contributed to the lower return-to-work rate. These findings suggest the potential for prolonged exocrine impairment and highlight the need for long-term evaluation.

Our study has some limitations. First, we only analyzed Japanese adult patients, and cultural, occupational, and healthcare system differences may limit generalizability to other regions. Second, patients who were unable to provide informed consent or complete the questionnaire at admission, as well as those who died or were lost to follow-up before the 3-month visit, were excluded from this study. Consequently, selection bias was unavoidable.

In conclusion, more than 20% of patients with acute pancreatitis experienced incomplete return to work at 3 months, which was associated with a higher frequency of impaired physical HRQoL than that of those with complete return. Causal analysis identified female sex, disease severity on admission, and reduced subjective HRQoL as contributing to incomplete return at 3 months. At 12 months, incomplete return to work remained prevalent, especially among females, regardless of disease severity. These results suggest the need for early physical recovery support and later-stage attention to psychosocial and occupational reintegration in Japan.

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Specific Author Contributions:

Conceptualization: Masayuki Ueno, and Yoshihisa Tsuji; Methodology: Masayuki Ueno, Yoshihisa Tsuji, Etsuji Ishida, Hironobu Tokumasu, and Motowo Mizuno; Formal analysis and investigation: Masayuki Ueno, Yoshihisa Tsuji, Ayako Hata, and Hironobu Tokumasu; Writing–original draft preparation: Masayuki Ueno, and Yoshihisa Tsuji; Writing–review and editing: Takaaki Eguchi, Akihisa Fukuda, Yusuke Kurita, Yukiko Takayama, Yugo Sawai, Takashi Tamura, Mamoru Takenaka, Tetsuhiro Atono, Hidenori Tanaka, Atsushi Masamune, Satoshi Yamamoto, Keisuke Ishigami, Toshihiro Kusaka, Hiroki Kawashima, Nobuhiko Hayashi, Ayako Hata, Etsuji Ishida, Hironobu Tokumasu, Norimitsu Uza, Hiroshi Seno, Hiroki Yamaue, Sohei Satoi, Yoshifumi Takeyama, Kazuichi Okazaki, and Motowo Mizuno; Funding acquisition: Masayuki Ueno; Supervision: Hiroshi Seno, Hiroki Yamaue, Sohei Satoi, Yoshifumi Takeyama, Kazuichi Okazaki, and Motowo Mizuno.

Declaration of interests: None declared.

Data availability statement: The data that support the findings of this study are available on request from the corresponding author, YT. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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Tables

Table 1. Comparison of the characteristics and treatments between patients with complete and incomplete return to work at 3 months post-onset

Categories	Total patients (n = 226)	Return to work		p value	
		Complete (n = 177)	Incomplete (n = 49)		
Age, years	67 [52–75]	67 [50–75]	67 [57–75]	0.48	
Sex	Male	149 (65.9)	122 (68.9)	27 (55.1)	0.10
	Female	77 (34.1)	55 (31.1)	22 (44.9)	
Body mass index on admission, kg/m ²	23.3 [20.6–26.5]	23.5 [20.8–26.6]	22.6 [20.3–25.2]	0.30	
Etiology	Gallstone	73 (32.3)	60 (33.9)	13 (26.5)	0.28
	Idiopathic	56 (24.8)	47 (26.6)	9 (18.4)	
	Alcohol	35 (15.5)	25 (14.1)	10 (20.4)	
	Others	62 (27.4)	45 (25.4)	17 (34.7)	
Baseline SF-12 scores	PCS	45.8 ± 11.9	47.2 ± 11.5	40.9 ± 12.0	<0.01**
	MCS	56.8 ± 9.5	57.2 ± 9.1	55.7 ± 11.0	0.33
	RCS	49.9 ± 10.2	51.0 ± 9.4	46.1 ± 11.9	<0.01**
	Mild	178 (78.8)	146 (82.5)	32 (65.3)	
Revised Atlanta criteria	Moderately severe	31 (13.7)	20 (11.3)	11 (22.4)	0.01*
	Severe	17 (7.5)	11 (6.2)	6 (12.2)	
JPN criteria on admission	Mild	138 (61.1)	114 (64.4)	24 (49.0)	0.07†
	Severe	88 (38.9)	63 (35.6)	25 (51.0)	
JPN prognostic factor	1 [0–1]	1 [0–1]	1 [0–2]	0.08	
APACHE II score on admission	7 [5–9]	6 [5–8]	8 [5–11]	<0.01**	
Charlson comorbidity index on admission	4 [2–5]	3 [2–5]	4 [3–5]	0.24	
Development of DIC	8 (3.5)	2 (1.1)	6 (12.2)	<0.01**	
Maximum value of CRP during hospitalization, mg/dL		11.0 [5.1–21.5]	10.8 [3.9–19.7]	13.1 [5.6–23.4]	0.20
	Total	36 (15.9)	24 (13.6)	12 (24.5)	0.08†
Development of local complications	Sterile ANC	26 (11.5)	20 (11.3)	6 (12.2)	0.80
	Infected ANC	1 (0.4)	0 (0)	1 (2.0)	0.22
	Sterile WON	4 (1.8)	2 (1.1)	2 (4.1)	0.21
	Infected WON	4 (1.8)	1 (0.6)	3 (6.1)	0.03*
	Sterile PPC	1 (0.4)	1 (0.6)	0 (0)	-
Length of hospitalization, days	10 [7–14]	9 [7–13]	12 [10–18]	<0.01**	
ICU care	9 (4.0)	4 (2.3)	5 (10.2)	0.04*	

Mechanical ventilator support		5 (2.2)	2 (1.1)	3 (6.1)	0.12
Surgical treatment		3 (1.3)	2 (1.1)	1 (2.0)	1.00
ERCP		60 (26.5)	49 (27.7)	11 (22.4)	0.58
Enteral nutrition		20 (9.8)	12 (6.8)	8 (16.3)	0.07†
Time from admission to oral feeding (hours)	<24	26 (11.5)	23 (13.0)	3 (6.1)	0.06†
	24–47	76 (33.6)	62 (35.0)	14 (28.6)	
	48–71	60 (26.5)	46 (26.0)	14 (28.6)	
	≥72	64 (28.3)	46 (26.0)	18 (36.7)	
Interventions to local complications		4 (1.8)	1 (0.6)	3 (6.1)	0.05*
Total costs for in-hospital treatment	Japanese yen (×1,000)	577 [418–908]	543 [400–832]	661 [561–1,282]	<0.01**

Continuous variables were presented as either mean \pm SD for parametric data or median [interquartile range] for non-parametric data. Comparisons were performed using Student's t-test for parametric data and the Mann–Whitney U test for non-parametric data.

“†”, “*”, and “**” represents $p < 0.1$, $p < 0.05$, and $p < 0.01$, respectively.

ANC, acute necrotic collection; APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index; CRP, C-reactive protein; DIC, disseminated intravascular coagulation; ERCP, endoscopic retrograde cholangiopancreatography; ICU, intensive care unit; JPN, Japanese; MCS, mental component score; PCS, physical component score; PPC, pancreatic pseudocyst; RCS, role-social component score; SF, Short-Form Health Survey; WON, walled-off necrosis.

Table 2. Binomial logistic analysis on factors associated with incomplete return to work at 3 months post-onset

	Explanations	Odds ratio	Two-sided 95% confidence interval		<i>p</i> value
			Lower limit	Upper limit	
(Intercept)		0.03	0.001	1.90	0.10†
Age		0.98	0.93	1.04	0.53
Sex	(Male 0, Female 1)	3.58	1.30	9.83	0.01*
Body mass index	(kg/m ²)	0.96	0.86	1.08	0.55
SF-12 scores	delta PCS (Difference between pre-scores and 3-month scores)	0.96	0.92	1.01	0.08†
	delta MCS	0.97	0.92	1.02	0.21
	delta RCS	0.95	0.91	0.99	0.01*
Revised Atlanta criteria	(Mild 0, Moderately severe 1, Severe 2)	1.47	0.34	6.37	0.61
JPN criteria	(Mild 0, Severe 1)	1.20	0.38	3.75	0.76
JPN prognostic factor		0.62	0.29	1.32	0.21
APACHE II score		1.33	1.10	1.60	<0.01**
Charlson comorbidity index		1.09	0.71	1.68	0.69
ICU care	(Negative 0, Positive 1)	0.23	0.01	3.97	0.31
Maximum CRP		1.02	0.97	1.08	0.40
Subjective HRQoL	(Improved -1, Unchanged 0, Slightly worsened 1, Worsened 2)	33.90	11.20	102.00	0.05*

Categorical variables were converted into dummy variables.

“†”, “*”, and “**” represents $p < 0.1$, $p < 0.05$, and $p < 0.01$, respectively.

APACHE II, Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein; HRQoL, health-related quality of life; ICU, intensive care unit; JPN, Japanese; MCS, mental component score; PCS, physical component score; RCS, role-social component score.

Figure Legends

Figure 1. Study schema and comparison of HRQoL between patients with complete and incomplete return to work at 3 months post-onset

a. Schematic representation of participants' enrollment. On the basis of follow-up status at 3 and 12 months, 226 and 211 patients were included, respectively. The areas enclosed by dashed lines represent the 3- and 12-month cohorts, respectively.

b. Comparison of SF-12 scores (PCS, MCS, and RCS) between baseline and 3-month values.

c. Comparison of SF-12 domain scores between baseline and 3-month values.

d. Return-to-work status at 3 months.

e. Comparison of PCS, MCS, and RCS changes (delta scores) from baseline to 3 months between patients with complete and incomplete return to work.

f. Comparison of proportions of patients with incomplete return to work between patients with maintained/improved and worsened subjective HRQoL. Patients with "worsened" or "slightly worsened" overall HRQoL were classified as "worsened," and those with "unchanged" or "improved" were classified as "maintained/improved."

"*" and "***" represents $p < 0.05$ and $p < 0.01$, respectively.

AP, acute pancreatitis; HRQoL, health-related quality of life; PCS, physical component score; MCS, mental component score; RCS, role-social component score.

Figure 2. Results of causal analysis in the 3-month cohort

Arrows indicate the causal relationships between causes and effects. The numbers [] indicate causal effects [bootstrap probability]. Red lines represent significant effects with a bootstrap probability ≥ 0.95 .

Figure 3. Comparison of HRQoL between patients with complete and incomplete return to work at 12 months post-onset

a. Return-to-work status at 12 months.

b. Comparison of SF-12 scores (PCS, MCS, and RCS) between baseline and 12-month values.

c. Comparison of PCS, MCS, and RCS changes (delta scores) from baseline to 12 months between patients with complete and incomplete return to work.

d. Comparison of proportions of patients with incomplete return to work with maintained/improved and worsened subjective HRQoL at 12 months. Patients with "worsened" or "slightly worsened" overall HRQoL were classified as "worsened," and those with "unchanged" or "improved" were classified as "maintained/improved."

e. Results of causal analysis in the 12-month cohort. Arrows indicate the causal relationships between causes and effects. The numbers [] indicate causal effects [bootstrap probability]. Red lines represent significant effects with a bootstrap probability ≥ 0.95 .

"*" and "***" represents $p < 0.05$ and $p < 0.01$, respectively.

HRQoL, health-related quality of life; PCS, physical component score; MCS, mental component score; RCS, role-social component score.

Figure 1

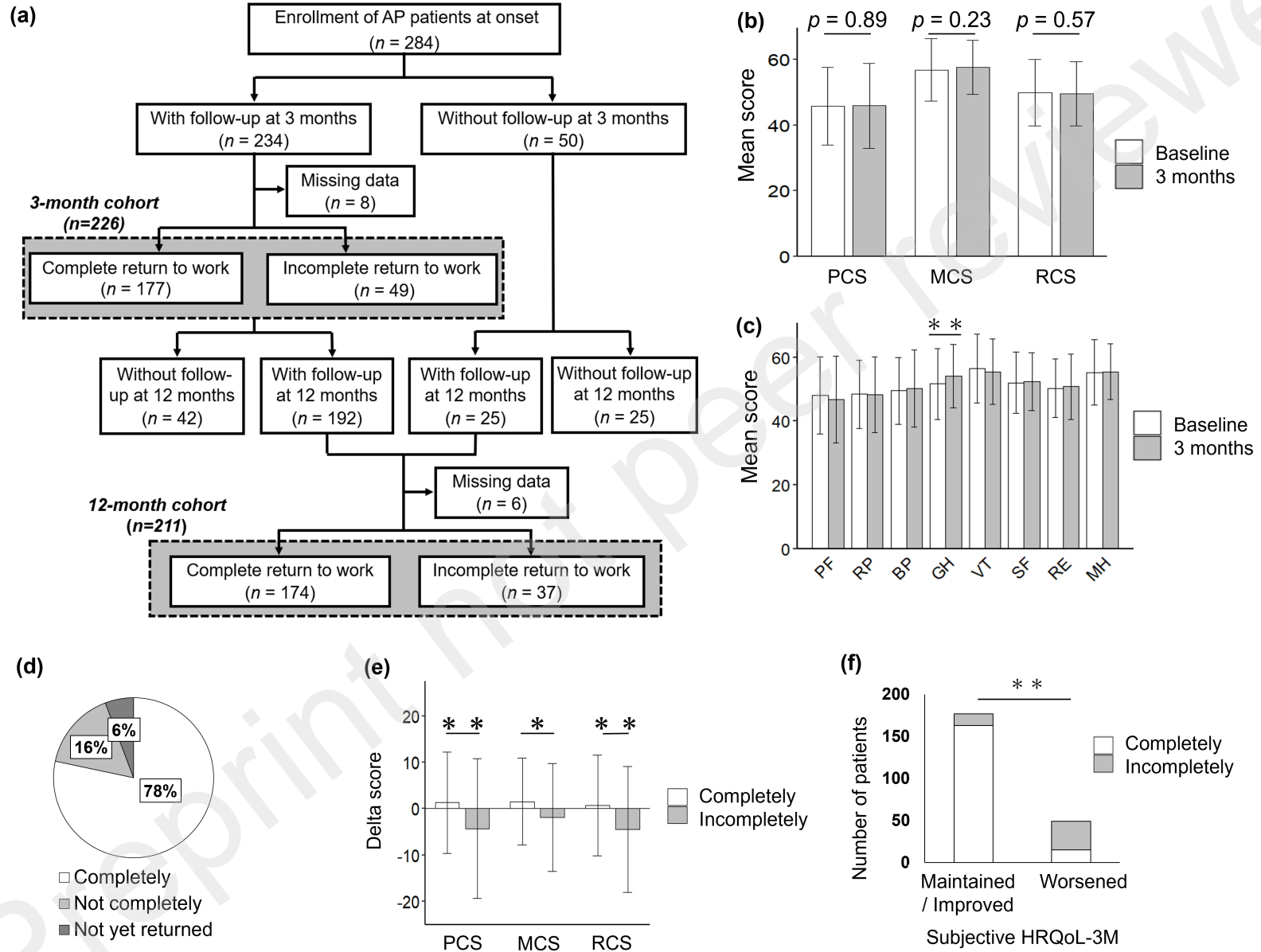


Figure 2

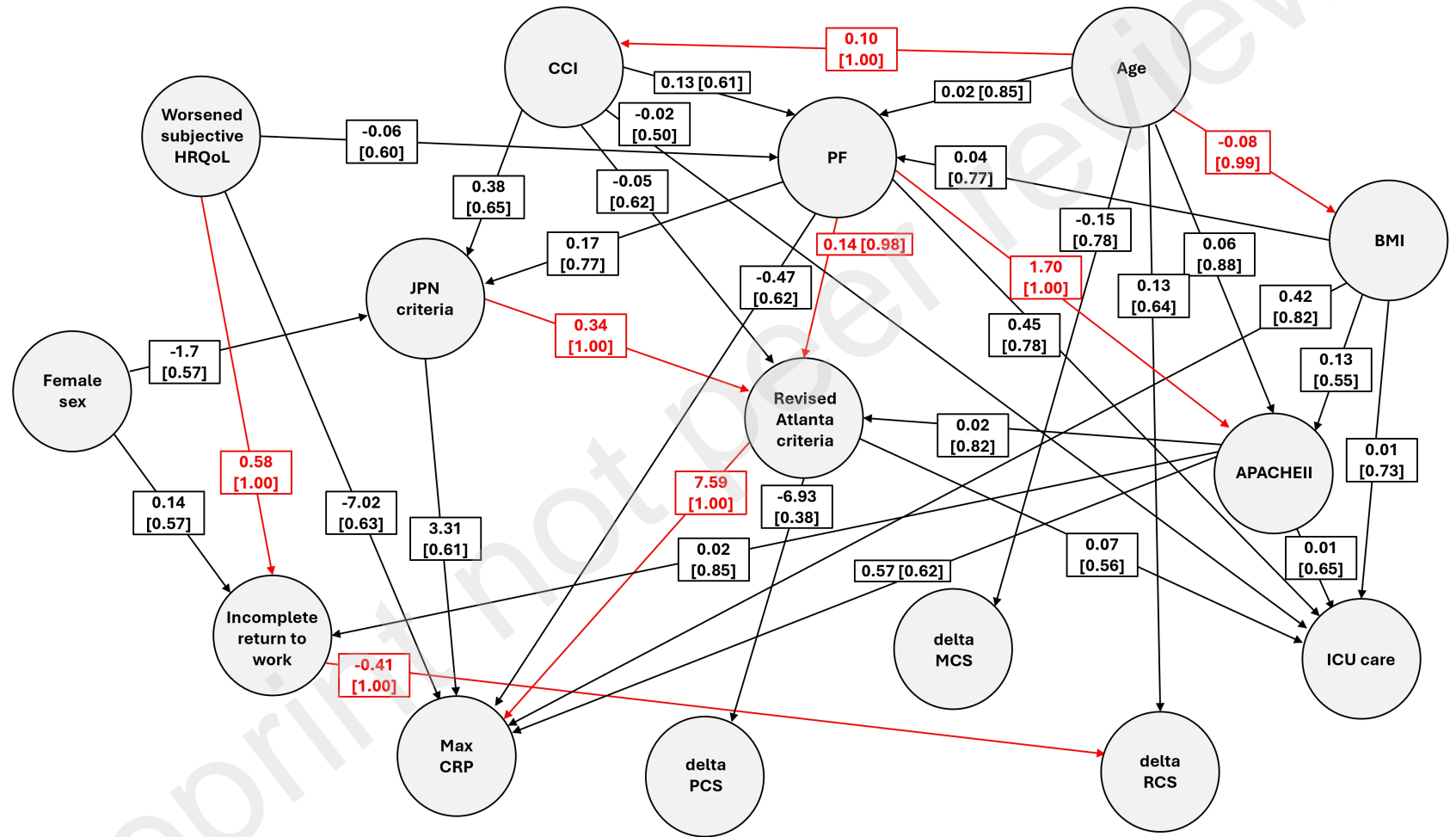
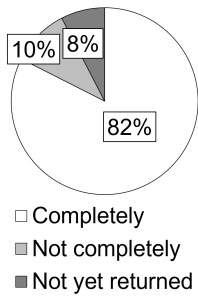
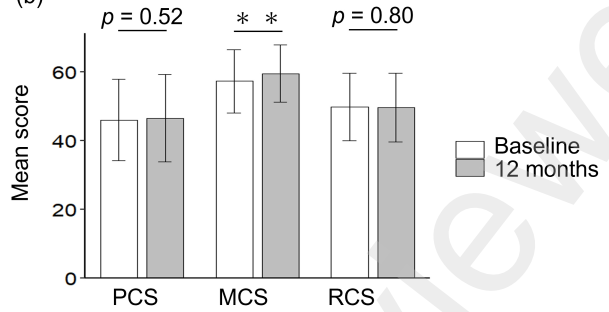


Figure 3

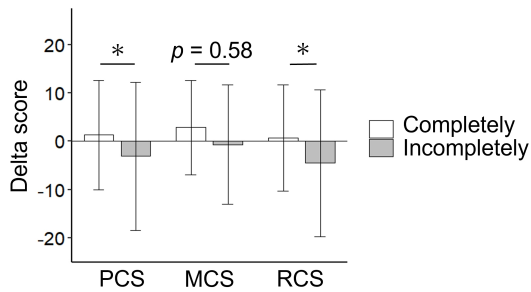
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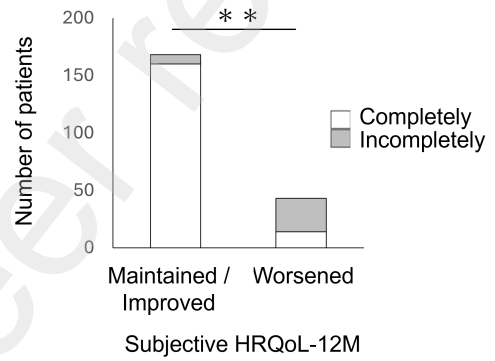
(b)



(c)



(d)



(e)

