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Original Article

Early invasive mechanical ventilation improves 28-day clinical outcomes in patients with severe pneumonia complicated by gastrointestinal dysfunction

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Abstract: Objectives: To investigate the impact of the timing of invasive mechanical ventilation (IMV) on 28-day clinical outcomes in patients with severe pneumonia (SP) complicated by gastrointestinal dysfunction. Methods: This retrospective study enrolled 104 patients with SP and gastrointestinal dysfunction who received IMV. Based on the time from meeting IMV criteria to its initiation, patients were divided into an Early Group (≤6 hours, n = 52) and a Delayed Group (>6 hours, n = 52). Clinical efficacy, scores [Clinical Pulmonary Infection Score, Acute Physiology and Chronic Health Evaluation II (APACHE II), Gastrointestinal Dysfunction Score (GIDS)], inflammatory markers [C-reactive protein (CRP), Tumor necrosis factor-α (TNF-α), Procalcitonin (PCT)], blood gas parameters [Oxygenation index (PaO_2/FiO_2) and Arterial partial pressure of oxygen (PaO_2)], gastrointestinal function, and prognosis were compared. Results: The total effective rate was significantly higher in the Early Group (86.54%) than that in the Delayed Group (76.92%) ($P<0.05$). Intergroup comparisons at 48 and 72 hours post-IMV revealed that the Early Group demonstrated superior improvement in APACHE II scores, GIDS, blood gas parameters, inflammatory markers, and gastrointestinal markers [Gastrin (GAS), Diamine oxidase (DAO)] (all $P<0.05$). Furthermore, the Early Group had a higher 28-day survival probability, shorter ICU stay and ventilation duration, and a significantly lower overall incidence of adverse reactions (19.23% vs. 53.84%) ($P<0.05$). Conclusions: For patients with SP and gastrointestinal dysfunction, early IMV initiation within 6 hours is more effective in mitigating systemic inflammation, improving blood gas exchange and gastrointestinal function, optimizing infection control, reducing adverse events, and ultimately improving clinical prognosis.

Keywords: Severe pneumonia, invasive mechanical ventilation, gastrointestinal dysfunction, treatment timing

Introduction

Severe pneumonia (SP) is an infectious lesion of the pulmonary parenchyma caused by pathogens. When pulmonary tissue inflammation progresses, it can lead to organ dysfunction and even life-threatening conditions, making it a common critical illness in intensive care units (ICU) and other settings. The condition is primarily characterized by symptoms such as dyspnea, hypoxemia, and increased pulmonary rales. As the disease advances, it may give rise to severe complications including multiple organ dysfunction and septic shock, which can be fatal [1]. Research indicates a high incidence of complications, including the circulatory, digestive, and coagulation systems [2]. Notably, among the SP-induced multisystem impairments, gastrointestinal dysfunction is particularly prominent, with an incidence rate as high as 60% [3]. This is mainly attributed to intestinal mucosal ischemic and hypoxic injury resulting from systemic hypoxia and severe infection. Concurrently, elevated intra-abdominal pressure further exacerbates respiratory function and oxygenation status. The deteriorated condition may trigger systemic organ failure, significantly increasing the risk of mortality.

At present, for SP patients complicated by gastrointestinal dysfunction, comprehensive treatment approaches are mainly adopted in clinical practice, including respiratory support, nutritional support, anti-infective therapy, and gastrointestinal motility promotion [4]. Among the-

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se, respiratory support is a key component of the treatment system, patients with this condition often fall into a vicious cycle of "respiratory failure-gastrointestinal injury" due to severe hypoxia and ventilatory failure. Respiratory support can directly block this cycle by rapidly improving oxygenation and relieving respiratory muscle fatigue, thereby creating basic conditions for subsequent treatments such as anti-infective therapy and gastrointestinal function repair. As a core and commonly used method in respiratory support for moderate-to-severe respiratory failure, invasive mechanical ventilation (IMV) plays an irreplaceable role in correcting severe hypoxemia, optimizing gas exchange, and reducing the persistent damage of systemic hypoxia to the gastrointestinal mucosa. Relevant clinical researchers [5] have found that initiating IMV within 6 hours of the appearance of mechanical ventilation indications can minimize the duration of assisted ventilation and hospital stay, while reducing the complication risks such as ventilator-associated pneumonia, resulting in better treatment efficacy. However, there are still controversies among different scholars regarding the selection of IMV treatment timing for such patients. Given that the timing of IMV is directly related to the oxygenation improvement rate gastrointestinal function recovery process, and overall patient prognosis, clarifying the optimal intervention timing is of great clinical guiding value for further treatment efficacy improvement of SP patients complicated by gastrointestinal dysfunction and severe complication reduction.

Based on this, the present study compares the effects of different timing of IMV on clinical outcomes including 28-day in-hospital mortality, ICU length of stay, airway inflammatory biomarkers, and gastrointestinal function parameters in SP patients complicated by gastrointestinal dysfunction. It aims to address the ongoing controversy regarding the optimal timing of respiratory support, identify a superior IMV strategy, and thereby offer evidence-based guidance for improving patient prognosis and optimizing clinical management.

Material and methods

Case selection

The sample size calculation was estimated based on $\alpha = 0.05$ (two-tailed test) and $1\text{-}\beta = 80\%$. According to the results of the preliminary experiment, p1 was expected to be 45% and p2 = 75%, with a 1:1 sample size ratio between the two groups. Based on PASS 15.0 software, 38 cases were required for each of the early group and the delayed group. Considering a 20% attrition rate, the total sample size was determined to be 96 cases, with 48 cases in each group. A total of 104 SP patients complicated by gastrointestinal dysfunction admitted to the inpatient department of Ningbo Zhenhai Hospital of Traditional Chinese Medicine from September 2022 to February 2025 were retrospectively enrolled in this study. The enrolled patients were divided into an early group (IMV within 6 h, n = 52) and a delayed group (IMV after 6 h, n = 52). This study was approved by the ethics committee of Ningbo Zhenhai Hospital of Traditional Chinese Medicine (Ethical approval number: LWSL-2025-01). All data were de-identified to protect patients' privacy, and all methods were conducted in accordance with the regulations of the relevant clinical ethics committee and the ethical guidelines of the World Medical Association (Declaration of Helsinki).

Diagnostic criteria: Diagnostic criteria for SP were based on the clinical practice guidelines of the American Thoracic Society/Infectious Diseases Society of America [4]. SP may be diagnosed when a patient meets one major criterion or three or more minor criteria based on the following diagnostic criteria: Major criteria included: (1) requirement for tracheal intubation for IMV, and (2) septic shock requiring vasoactive agents even after active fluid resuscitation. Minor criteria included: (1) respiratory rate (RR) ≥30 breaths/min, (2) oxygenation index (arterial partial pressure of oxygen (PaO_2)/FiO_2) ≤250 mmHg (1 mmHg = 0.133 kPa), (3) multilobar pulmonary infiltration, (4) disturbance of consciousness and/or disorientation, (5) blood urea nitrogen level ≥7.14 mmol/L, and (6) systolic blood pressure <90 mmHg requiring active fluid resuscitation. The Western medical diagnostic criteria for gastrointestinal dysfunction were established based on the 2012 European Society of Intensive Care Medicine consensus on acute gastrointestinal injury [6]. Diagnosis can be established when one or more of the following criteria are satisfied: (1) abdominal distension; (2) paralytic ileus; (3) reduced or absent bowel sounds (lasting >24 h); (4) constipation; (5) gastric retention.

Inclusion and exclusion criteria: Inclusion criteria: (1) Age ≥18 years old; (2) Comprehensive evaluation by the attending physician based on admission vital signs, disease severity, comorbidities, and organ function, with an expected survival time ≥72 hours; (3) Met the diagnostic criteria for both SP and gastrointestinal dysfunction; (4) Able to closely cooperate with treatment and follow-up procedures; (5) Complete clinical data available.

Exclusion criteria: (1) Gastrointestinal perioperative period (within 1 month before enrollment) or active gastrointestinal bleeding; (2) Pregnant or lactating women; (3) Concurrent participation in other clinical trials; (4) Complicated with severe primary diseases, such as cardiovascular, cerebrovascular, liver, kidney, coagulation system and other diseases; (5) Advanced malignant tumors, severe immune system defects and other diseases; (6) Nervous system diseases that preclude cooperation with researchers.

Intervening methods

After admission, patients in both groups received routine symptomatic treatment, including relieving cough, relieving asthma, anti-infection, nutritional support, etc., and underwent IMV treatment. The ventilation modes used included Synchronized intermittent mandatory ventilation (SIMV) and Pressure-regulated volume control ventilation (PRVC). The tidal volume was set at 8-10 mL/kg, RR at 16-20 breaths/min, static expiratory-to-inspiratory ratio at 1:1.5-2.5, Fraction of inspired oxygen (FiO_2) at 35%-50%, and Pressure support ventilation (PSV) at 8-16 mmHg. These parameters were adjusted according to the patient's actual condition, symptoms, and blood gas analysis indicators. The specific weaning criteria were defined as follows: Effective control of the patient's primary disease with stable clinical status; recovery of spontaneous breathing capacity, characterized by a RR ≤30 breaths/min and a spontaneous tidal volume ≥5 mL/kg; arterial blood gas parameters meeting the following thresholds: PaO_2/FiO_2 ≥200 mmHg, arterial partial pressure of carbon dioxide ($PaCO_2$) maintained at the patient's baseline or within the normal physiological range; stable circulatory status, defined as no requirement for vasoactive agents or maintenance with only low-dose vasoactive medications; preserved consciousness with the ability to effectively cough and expectorate sputum.

Patients meeting the aforementioned criteria were eligible for a spontaneous breathing trial (SBT). Following successful SBT, ventilator support parameters were gradually titrated downward until ventilator weaning and subsequent extubation.

Data collection

General information: The data of this study were derived from the hospital electronic medical record system, and the required biological samples and detection methods strictly adhered to standardized operating procedures. General information included gender, age, disease course, and vital signs (heart rate, body temperature). To ensure data quality, standardized data extraction criteria were implemented in this study. Two researchers independently verified medical records, and disputed data were arbitrated by a third senior physician.

Prior to blood collection, patient information (name, hospital ID, and group assignment) was verified, and the sampling time points (before IMV, 48 hours, and 72 hours after IMV) were confirmed. Disposable vacuum blood collection tubes (dry tubes without anticoagulant, EDTA - K2 anticoagulant tubes, lithium heparin anticoagulant tubes), sterile blood collection needles, tourniquets, povidone-iodine disinfectant, sterile cotton swabs and other items were prepared, and all consumables met clinical testing standards. The antecubital vein was selected as the blood collection site, and sterile blood collection needles were used for venipuncture. After successful puncture, 2 mL of blood was first collected into EDTA - K2 anticoagulant tubes for the detection of White blood cell count (WBC) and neutrophil percentage (N%). Subsequently, 5 mL of blood was collected into dry tubes without anticoagulant, which were left to stand naturally for 30 minutes to allow blood coagulation, for the detection of C-reactive protein (CRP) and Procalcitonin (PCT). Finally, 3 mL of blood was collected into lithium heparin anticoagulant tubes, which were inverted and mixed 5 times, for the detection of Tumor necrosis factor-α (TNF-α). Gastrin (GAS) and Diamine oxidase (DAO) were detected using the corresponding Enzyme-linked immunosorbent assay (ELISA) kits. Meanwhile, radial artery blood was collected for blood gas analysis to detect PaO_2/FiO_2, PaO_2, and $PaCO_2$.

Follow-up: After IMV treatment, all patients received subsequent inpatient treatment in accordance with medical advice. They were instructed to receive routine exercise combined with diet, including breathing training, nebulized inhalation, and oxygen therapy adjustment. These measures aimed to prevent and control complications such as infection, and carry out limb training. Besides, gastrointestinal function regulation, supplementation, and comorbidity management were performed.

All patients underwent a 28-day follow-up, with re-examinations on Days 7, 14, and 28. Daily mortality in each group was recorded. Respiratory function, gastrointestinal function, and systemic status were evaluated. Meanwhile, adverse events and activity ability were recorded. Prognostic data were collected, and all information was entered into a pre-established database to ensure standardization and completeness.

Observation indicators

The primary outcome measures of this study was the 28-day mortality rate. Secondary outcomes were categorized as follows: (1) Comprehensive prognostic indicators (from IMV completion at enrollment to Day 28 post-enrollment): the 28-day survival with non-ICU hospital stay days (total days not in the ICU for patients surviving 28 days post-enrollment); 28-day survival with non-IMV days (total days without IMV for patients surviving 28 days post-enrollment) and time to ICU discharge for survivors (survivors only, duration from ICU admission to discharge (hours/days); patients who died or remained in the ICU at Day 28 were excluded). (2) Baseline data: Gender, age, disease course, heart rate (HR), body temperature. (3) Clinical efficacy evaluation: with the references of *Guidelines for the Evaluation and Treatment of Pneumonia* [7]. Markedly effective: Symptoms such as cough and expectoration were significantly improved, and moist rales and wheezes in both lungs basically resolved. Effective: The above symptoms were alleviated, and moist rales and wheezes in both lungs were improved. Ineffective: The above symptoms such as cough and expectoration showed no significant improvement or even worsened. Total effective rate = (Number of markedly effective cases + Number of effective cases)/Total number of cases × 100%. (4) Comparison of Clinical Pulmonary Infection Score (CPIS) [8], Acute Physiology and Chronic Health Evaluation II (APACHE II) score [9], and Gastrointestinal Dysfunction Score (GIDS) [10] between the two groups before and after IMV. CPIS: CPIS was used to assess the severity of pulmonary infection in patients. With a maximum score of 12 points, this scoring system includes 7 categories of indicators, such as progression of pulmonary infiltration, results of tracheal aspirate culture, and body temperature. A lower score indicates a milder degree of pulmonary infection. APACHE II Score: This scoring system consists of age score, acute physiology score, and chronic health status score. The age scoring criteria are as follows: ≤44 years old (0 points), 45-55 years old (2 points), 55-65 years old (3 points), 65-75 years old (5 points), and ≥75 years old (6 points). The acute physiology score is evaluated based on 12 parameters including RR, PaO_2, and creatinine concentration, with 0-4 points for each parameter. The chronic health status score is calculated based on kidney function, immune function, and surgical status. The total APACHE II score is the sum of the three parts, ranging from 0 to 71 points. A lower score indicates better health status of the patient. GIDS was used to assess gastrointestinal function impairment in patients before and after IMV. This score is divided into 5 grades, with a maximum score of 4 points. Normal gastrointestinal function is classified as Grade 0 (0 point); presence of mild nausea/vomiting (≤2 episodes/day), diminished bowel sounds, or Intra-abdominal pressure (IAP) of 12-15 mmHg is classified as Grade 1 (1 point). Occurrence of gastric retention, diarrhea, feeding intolerance (failure to achieve nutritional goals within 3 days), or IAP of 12-15 mmHg persisting for ≥24 h is classified as Grade 2 (2 points). Presence of persistent feeding intolerance (failure to achieve nutritional goals within 7 days), massive gastric retention, or IAP of 15-20 mmHg is classified as Grade 3 (3 points). Occurrence of intestinal ischemic necrosis, abdominal compartment syndrome (ACS, with IAP >20 mmHg), or complications with ≥3 other organs is classified as Grade 4 (4 points). (5) Inflammation-related indicators: The levels of CRP, TNF-α, PCT, WBC, and N% were detected in both groups before IMV and at 48 h and 72 h after IMV. (6) Blood gas analysis indicators: The levels of PaO_2/FiO_2, RR, PaO_2, and $PaCO_2$ were detected in both groups before IMV and at 48 h

Table 1. Comparison of general baseline data

Items	Early group (n = 52)	Delayed group (n = 52)	$Z/t/\chi^2$ value	*P*-value
Gender (n, %)			1.393	0.238
Male	21.00 (40.38)	27.00 (51.92)		
Female	31.00 (59.62)	25.00 (48.08)		
Age (years, $\bar{x}\pm s$)	77.83±12.91	71.06±11.35	0.001	0.975
Disease duration [years, *M* (P_{25}, P_{75})]	6.02 (5.83, 7.52)	5.78 (4.14, 6.74)	-0.356	0.722
Heart rate (HR) (beats/min, $\bar{x}\pm s$)	115.30±9.43	114.77±9.25	0.051	0.822
Body temperature (°C, $\bar{x}\pm s$)	37.75±1.15	37.55±1.41	3.651	0.060

Table 2. Comparison of clinical efficacy (n, %)

Group	Marked effective	Effective	Ineffective	Total effective rate
Early group (n = 52)	20.00 (38.46)	25.00 (48.08)	7.00 (13.46)	45.00 (86.54)
Delayed group (n = 52)	8.00 (15.38)	32.00 (61.54)	12.00 (23.08)	40.00 (76.92)
Z value				-2.529
P-value				0.011

and 72 h after IMV. (7) Gastrointestinal function indicators: The levels of GAS, DAO, AC, and IAP were measured in both groups before IMV and at 48 h and 72 h after IMV. (8) Acute Respiratory Distress Syndrome (ARDS) progression incidence indicator: Incidence of progression to ARDS was recorded during ICU hospitalization [11]. (9) Adverse reactions: The adverse reactions occurring in both groups during treatment, including nausea, dizziness, headache, diarrhea, vomiting, etc., were recorded and compared. The total incidence of adverse reactions was calculated using the follow formula: Incidence of adverse reactions = (Number of patients with at least one adverse reaction ÷ Total number of patients in the group) × 100%.

Statistical analysis

SPSS version 27.0 software was used for data analysis in this study. The Shapiro-Wilk test was applied to verify the normality of continuous data. Continuous data that conformed to a normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± sd), and comparisons between the two groups were performed using the independent samples t-test. Continuous data that did not conform to a normal distribution were expressed as median (interquartile range, IQR) in the form of M (Q25, Q75), and comparisons between the two groups were conducted using the Mann-Whitney U test. Categorical data were presented as rates (%), and the chi-square (χ^2) test was used for comparisons. A repeated-measures analysis of variance (ANOVA) was used to assess the differences between the two groups across the three time points. The significance level (α) was set at 0.05, and a *P*-value <0.05 was considered statistically significant.

Results

Comparison of baseline characteristics

There were no significant differences between the groups in terms of gender, age, disease duration, heart rate, body temperature, and other parameters (all *P*>0.05). These results confirmed that the two groups demonstrated good comparability (**Table 1**).

Comparison of clinical efficacy

The total effective rate in the early group (86.54%) was significantly higher than that in the delayed group (76.92%) (*P*<0.05, **Table 2**).

Comparison of CPIS, APACHE II, and GIDS scores

Prior to IMV, there were no significant differences in CPIS, APACHE II, or GIDS scores between the two groups (all *P*>0.05). Compared with pre-IMV values, both groups exhibited significant reductions in CPIS and GIDS scores at 48 h and 72 h post-ventilation, while APACHE II scores showed significant reduction only at 72 h post-ventilation (all *P*<0.05). Between 48 h

Table 3. Comparison of CPIS, APACHE II and GIDS scores ($\bar{x}\pm s$)

Indications	Time period	Early group (n = 52)	Delayed group (n = 52)	*t*-value	*P*-value
CPIS	Pre-MV	5.53±1.67	5.73±1.31	-0.598	0.552
	48 h post-MV	4.45±1.32*	4.70±1.12*	-0.897	0.372
	72 h post-MV	3.11±1.24*,#	4.67±1.67*	-4.771	<0.001
	F-value	28.974	7.418		
	P-value	<0.001	0.001		
	Between-Subjects Effect		*F* = 14.098; *P*<0.001		
	Within-Subjects Effect		*F* = 30.756; *P*<0.001		
	Interaction		*F* = 6.094; *P* = 0.003		
APACHE II	Pre-MV	22.23±5.92	23.10±5.45	-0.692	0.491
	48 h post-MV	20.31±3.44	25.15±4.07	-0.574	<0.001
	72 h post-MV	11.45±2.45*,#	20.35±3.55*,#	-13.050	<0.001
	F-value	85.191	11.642		
	P-value	<0.001	<0.001		
	Between-Subjects Effect		*F* = 76.117; *P*<0.001		
	Within-Subjects Effect		*F* = 66.395; *P*<0.001		
	Interaction		*F* = 17.342; *P*<0.001		
GIDS	Pre-MV	7.03±0.67	7.22±0.85	-1.116	0.268
	48 h post-MV	4.46±0.49*	6.22±0.88*	-11.113	<0.001
	72 h post-MV	3.46±0.43*,#	5.53±1.00*,#	-11.998	<0.001
	F-value	428.769	38.075		
	P-value	<0.001	<0.001		
	Between-Subjects Effect		*F* = 176.565; *P*<0.001		
	Within-Subjects Effect		*F* = 269.061; *P*<0.001		
	Interaction		*F* = 38.149; *P*<0.001		

Notes: CPIS: Clinical Pulmonary Infection Score; APACHE II: Acute Physiology and Chronic Health Evaluation II; GIDS: Gastrointestinal Dysfunction Score; *P<0.05 vs. pre-mechanical ventilation in the same group; #P<0.05 vs. 48 h post-mechanical ventilation in the same group.

and 72 h post-ventilation, both groups demonstrated further significant decreases in APACHE II and GIDS scores, with CPIS scores showing significant reduction only in the early group (all P<0.05). Inter-group comparison revealed that, compared with the delayed group, the early group had significantly lower APACHE II and GIDS scores at both 48 h and 72 h post-ventilation, with CPIS scores showing significant reduction only at 72 h post-ventilation (all P<0.05, **Table 3**).

Comparison of airway inflammation-related indicators

Before IMV, no statistically significant differences were observed in the levels of CRP, TNF-α, PCT, WBC, and N% between the two groups (all P>0.05). Compared with those before IMV, the levels of CRP, TNF-α, PCT, and N% in both groups were significantly decreased at 48 h and 72 h after IMV (all P<0.05). The WBC level was significantly decreased in the early group (P<0.05), while in the delayed group, a significant decrease was only observed at 72 h after IMV (P<0.05). Compared with those at 48 h after IMV, the levels of CRP, TNF-α, PCT, and N% in both groups were significantly decreased at 72 h after IMV, and the WBC level showed a significant decrease only in the delayed group (all P<0.05). Further inter-group comparison showed that, compared with the delayed group, the levels of CRP, TNF-α, PCT, and WBC in the early group were significantly decreased, while the N% level was significantly decreased only at 72 h after IMV (all P<0.05, **Figure 1**).

Comparison of blood gas analysis indicators

Before IMV, there were no statistically significant differences in the levels of PaO_2/FiO_2, RR, PaO_2, and $PaCO_2$ between the two groups (all

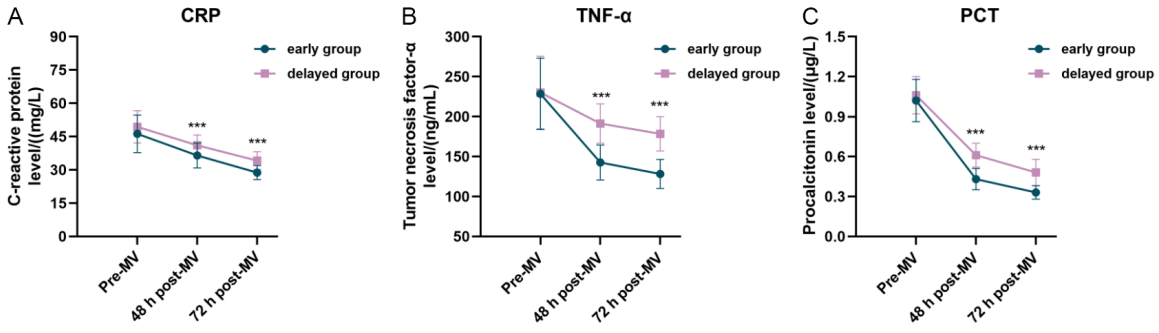

Figure 1. Comparison of airway inflammation-related indicators. Note: CRP: C-reactive protein; TNF-α: Tumor necrosis factor-α; PCT: Procalcitonin; WBC: White blood cell count; N%: Neutrophil percentage; A: Changes in CRP level; B: Changes in TNF-α level; C: Changes in PCT level; D: Changes in WBC level; E: Changes in N% level; *: $P<0.05$; **: $P<0.01$; ***: $P<0.001$.

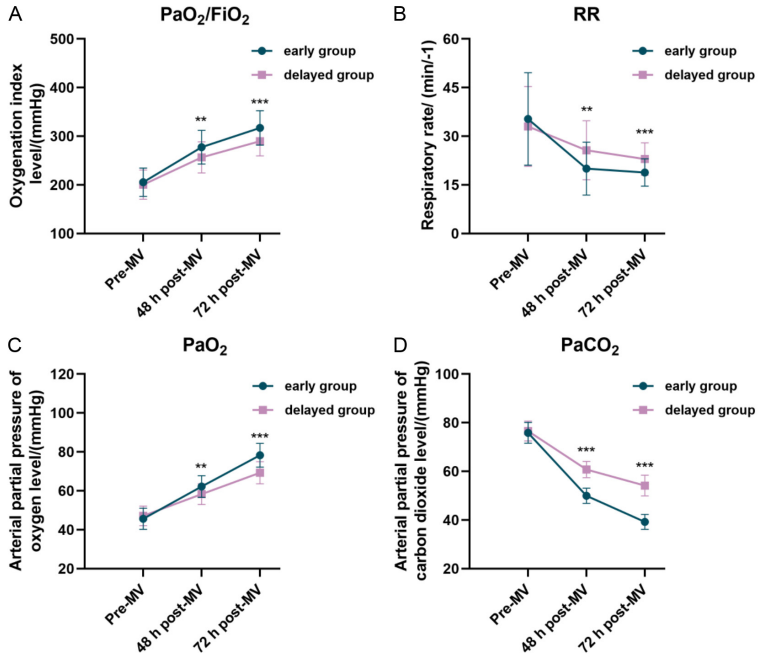

Figure 2. Comparison of blood gas analysis indicators. Note: PaO_2/FiO_2: Oxygenation index; RR: Respiratory rate; PaO_2: Arterial partial pressure of oxygen; $PaCO_2$: Arterial partial pressure of carbon dioxide; A: Changes in PaO_2/FiO_2 level; B: Changes in RR level; C: Changes in PaO_2 level; D: Changes in $PaCO_2$ level; **: $P<0.01$; ***: $P<0.001$.

$P>0.05$). Compared with those before IMV, the levels of PaO_2/FiO_2 and PaO_2 in both groups were significantly increased at 48 h and 72 h after IMV, while the levels of RR and $PaCO_2$ were significantly decreased compared with those in the same group before IMV (all $P<0.05$). Compared with those at 48 h after IMV, the levels of PaO_2/FiO_2 and PaO_2 in both groups were significantly increased at 72 h after IMV, and the RR level was significantly decreased (all $P<0.05$). Further inter-group comparison revealed that, compared with the delayed group, the early group had higher levels of PaO_2/FiO_2 and PaO_2, and lower levels of RR and $PaCO_2$ at 48 h and 72 h after IMV (all $P<0.05$, **Figure 2**).

Comparison of gastrointestinal function indicators

Before IMV, no statistically significant differences were observed in the levels of GAS, DAO, IAP, and AC between the two groups (all $P>0.05$). With the prolongation of time, the levels of GAS, DAO, IAP, and AC in both groups showed a decreasing trend, and the early group exhibited a more remarkable decreasing amplitude (all $P<0.05$). At 48 h, the levels of GAS,

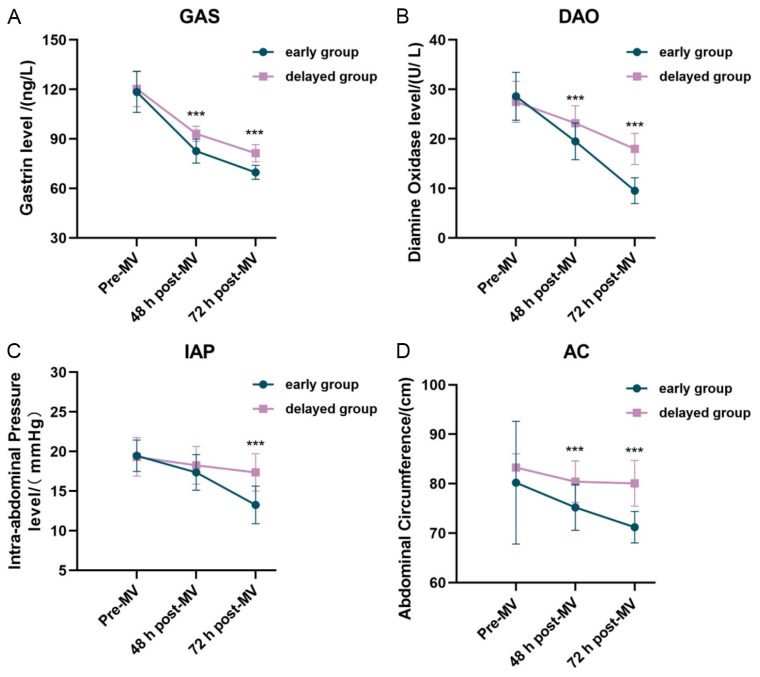

Figure 3. Comparison of gastrointestinal function. Note: GAS: Gastrin; DAO: Diamine oxidase; IAP: Intra-abdominal pressure; AC: Abdominal Circumference; A: Changes in GAS level; B: Changes in DAO level; C: Changes in IAP level; D: Changes in AC level; ***P<0.001.

Table 4. Comparison of progression to ARDS during ICU stay

Group	n	Incidence of ARDS (%)
Early group	52	17.00 (32.69)
Delayed group	52	27.00 (51.92)
χ^2-value		3.939
P-value		0.047

Note: ARDS: Acute Respiratory Distress Syndrome; ICU: intensive care units.

DAO, and AC in the early group were significantly lower than those in the delayed group (all P<0.05), whereas no significant difference was found in IAP levels between the two groups (P>0.05). At 72 h, the levels of GAS, DAO, IAP, and AC in the early group were significantly lower than those in the delayed group (all P<0.05, **Figure 3**).

Comparison of progression to ARDS during ICU stay

In the early group, 17 patients progressed to ARDS during ICU stay, with an incidence rate of 32.70%. In the delayed group, 27 patients progressed to ARDS during ICU stay, with an incidence rate of 51.90%. Statistical analysis showed that the incidence of ARDS in the early group was significantly lower than that in the delayed group (P<0.05, **Table 4**).

Comparison of prognostic outcomes

Compared with the delayed group, the early group demonstrated a significantly longer duration of non-ICU hospital stay, more ventilator-free days, a shorter ICU length of stay, and a lower 28-day mortality rate (all P<0.05) (**Table 5**). The 28-day survival curves of the two groups are shown in **Figure 4**. Survival analysis results showed that there was a statistically significant difference in survival probability between the early group and the delayed group during the follow-up period of this study (P<0.05). The survival curve of the early group was consistently above that of the delayed group. At all corresponding time points, the early group had a higher survival probability, while the delayed group showed a higher risk of death during the observation period of this study.

Comparison of adverse reactions

During treatment, the total incidence of adverse reactions in the early group was 19.23%, which was significantly lower than that in the delayed group at 53.85% (P<0.05, **Table 6**).

Discussion

As a clinically common high-risk critical illness, SP shows a steady upward incidence trend amid the growing aging of the population. It is frequently complicated by gastrointestinal dysfunction, which significantly increases the risk of multisystem impairment [12]. Gastrointestinal dysfunction is not only a prevalent complication of SP but also a well-established key trigger for systemic inflammatory response syndrome (SIRS); it can further induce sepsis and ARDS, ultimately progressing to irreversible organ failure and thus emerging as a core link influencing patient prognosis [13].

Table 5. Comparison of prognostic outcomes

Prognostic outcomes	Early group (n = 52)	Delayed group (n = 52)	t/χ^2-value	*P*-value
Days of non-ICU hospitalization among 28-day survivors (d)	13.54±2.45	10.53±3.14	5.451	<0.001
Days free of mechanical ventilation among 28-day survivors (d)	10.25±1.55	8.95±1.65	4.165	<0.001
Time to ICU discharge among survivors (d)	10.16±1.55	14.48±2.12	-11.888	<0.001
28-day mortality rate (%)	6.00 (11.54)	14.00 (26.92)	3.962	0.047

Note: ICU: intensive care units.

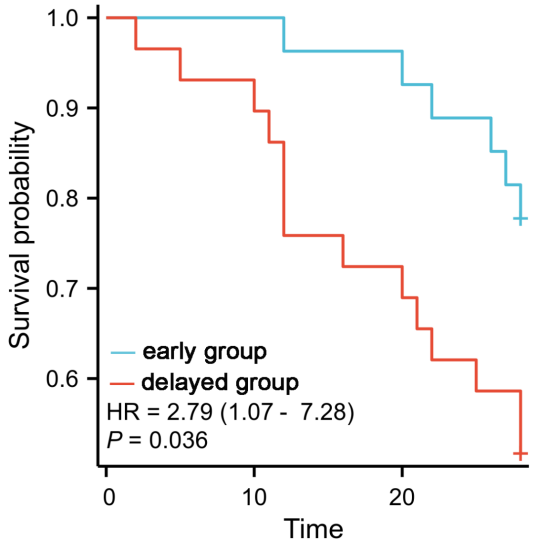

Figure 4. 28-day survival curves.

In the management of SP patients complicated with gastrointestinal dysfunction, although IMV can quickly correct hypoxemia, improve ventilatory function, and serve as an effective intervention for relieving respiratory symptoms [14, 15], controversy persists regarding the optimal timing of its initiation, which is an issue of particular clinical significance in this specific patient population. On one hand, although current Western medical therapies can effectively control SP-related infections, they have notable limitations in repairing impaired gastrointestinal function. On the other hand, inappropriate IMV initiation timing in some patients may further exacerbate gastrointestinal dysfunction, precipitating secondary severe complications such as intra-abdominal hypertension and abdominal compartment syndrome.

The results of this study demonstrated that early IMV (within 6 hours) significantly improved clinical outcomes compared to delayed intervention. The total clinical effective rate in the early group (86.54%) was significantly higher than that in the delayed group (76.92%), and the incidence of ARDS during ICU stay was significantly lower in the early group. Moreover, the ICU length of stay, duration of IMV, post-ICU hospital stay, and 28-day mortality were all significantly reduced in the early group. Survival analysis revealed a consistently higher survival probability in the early group throughout the follow-up period, which aligns with the previous findings [16]. In SP patients complicated by gastrointestinal dysfunction, initiating IMV within 6 hours can significantly shorten the duration of IMV and accelerate disease recovery through mechanisms such as effective drainage of airway secretions, ensuring adequate ventilation, promoting recovery of spontaneous breathing function, and alleviating respiratory-related symptoms. Conversely, failure to initiate effective ventilation beyond 6 hours may lead to increased risks of VAP, exacerbated disease progression, and compromised therapeutic efficacy of IMV due to rapid disease progression [17]. Therefore, implementing IMV within 6 hours after patients meet the indications for IMV can alleviate symptoms before rapid disease progression, ultimately achieving superior treatment outcomes.

Inflammatory response is a typical feature of pulmonary infection. Under normal circumstances, when pulmonary infection occurs, it activates the host immune system, promotes the release of inflammatory factors, and leads to a sharp increase in the levels of inflammatory factors [18]. When the patient is invaded by pathogenic bacteria, their hepatocytes are stimulated to a certain extent, triggering an acute response and resulting in a significant increase in the concentrations of inflammatory factors such as CRP, PCT, and TNF-α. Compared with the pre-IMV period, CRP, TNF-α, PCT, and N% were significantly decreased at 48 h and 72 h post-IMV in both groups. Notably, the early group exhibited a more rapid and pronounced reduction in WBC count, which

Table 6. Comparison of adverse reactions (n, %)

Group	Nausea	Dizziness	Headache	Diarrhea	Vomiting	Total
Early group (n = 52)	3.00 (5.80)	1.00 (1.90)	2.00 (3.80)	3.00 (5.80)	1.00 (1.90)	10.00 (19.23)
Delayed group (n = 52)	4.00 (7.70)	3.00 (5.80)	7.00 (13.50)	9.00 (17.30)	5.00 (9.60)	28.00 (53.85)
χ^2-value						14.496
P-value						0.013

decreased significantly by 48 h, whereas in the delayed group, a significant decrease was only observed at 72 h. The underlying reason may be that in the early group, IMV administered within 6 hours can recruit collapsed alveoli early, correct ventilation/perfusion (V/Q) imbalance, and reduce intrapulmonary shunting and tissue hypoxia - hypoxia activates hypoxia-inducible factor-1α (HIF-1α), which promotes the gene transcription and release of proinflammatory factors such as TNF-α and CRP [19]. IMV within 6 hours can directly inhibit this inflammatory initiation step by rapidly alleviating hypoxia. Meanwhile, maintaining lung functional residual capacity early can mitigate mechanical stretch injury to pulmonary epithelial cells and vascular endothelial cells, reduce the release of damage-associated molecular patterns (DAMPs) [20], and prevent DAMPs from further activating inflammatory cells like macrophages and neutrophils, thereby blocking the amplification of the inflammatory cascade. In contrast, the delayed group missed the early lung protection window, resulting in more significant alveolar edema, exudation, and epithelial barrier disruption. Not only was V/Q imbalance more pronounced, but continuous DAMP stimulation also led to increased accumulation of inflammatory factors. Consequently, the reduction in inflammatory indicators after IMV was limited in the delayed group, and the time for a significant decrease in WBC count was significantly later than in the early group. Further intergroup comparisons confirmed that the overall levels of the above indicators at 48 and 72 hours after ventilation in the early group were significantly lower than those in the delayed group, while N% was significantly lower than that in the delayed group only at 72 hours after ventilation. These findings suggest that early IMV treatment is more effective at reducing inflammatory factor levels and achieves faster and better anti-inflammatory effects, which is consistent with the research results of Forgiarini [21]. The mechanisms are as follows: Earlier IMV treatment can effectively dilate the patient's pulmonary blood vessels, help maintain the residual volume of lung function, thereby reducing intrapulmonary shunting and alleviating the inflammatory response caused by hypoxia [22, 23]. This suggests that clinically, for patients with pulmonary infection requiring IMV, evaluation should be prioritized, and every effort should be made to initiate IMV within 6 hours. By improving pulmonary physiological function and blocking inflammation progression as early as possible, the condition can be controlled more rapidly and persistent inflammatory damage to lung tissue can be reduced. This holds important practical guiding significance for reducing the risk of aggravated respiratory failure and improving the prognosis of patients.

When SP is complicated with gastrointestinal dysfunction, respiratory failure progresses rapidly and can cause airway spasm within a short period of time, leading to significant changes in blood gas indexes [24, 25]. This study showed that at 48 h and 72 h post-ventilation, both groups had significantly higher PaO_2/FiO_2 and PaO_2, and lower RR and $PaCO_2$ vs. pre-ventilation. Additionally, 72 h post-ventilation vs. 48 h, these indices further improved in both groups. This is consistent with the study by Yang. [26], suggesting that early treatment has a more prominent effect on improving patients' blood gas indexes. The underlying mechanism lies in the rapid progression of SP complicated with gastrointestinal dysfunction. IMV administered within 6 hours can recruit collapsed alveoli early by setting an appropriate level of positive end-expiratory pressure, reduce intrapulmonary shunting to improve gas exchange efficiency, and simultaneously clear airway secretions rapidly, relieve spasms, and reduce respiratory muscle load. These dual effects promote an increase in arterial PaO_2 and a decrease in RR, directly optimizing the oxygenation index [27]. In contrast, the delayed group, which received ventilation only after 6 hours, missed the alveolar protection window,

resulting in aggravated alveolar edema and an expanded range of alveolar collapse. There was no significant improvement in blood gas indices in the delayed group at 6 hours after ventilation initiation. The magnitude of oxygenation improvement was also lower at 48 hours and 72 hours thereafter. Additionally, the delayed group required higher ventilation parameters to maintain gas exchange, which increased the risk of ventilator-associated lung injury. Therefore, initiation of IMV within 6 hours can rapidly clear airway sputum, relieve airway spasm, improve respiratory muscle fatigue, and optimize gas exchange and ventilatory function. At the same time, it increases the body's arterial oxygen partial pressure, corrects hypoxemia, and creates favorable conditions for subsequent sequential treatment and prevention of VAP.

Studies have shown that abnormal secretion of gastrointestinal hormones is an important factor contributing to gastrointestinal dysfunction [28]. When the intestinal mucosal barrier is damaged, DAO produced by intestinal bacteria enters the bloodstream in large quantities through the damaged barrier. Therefore, DAO is often used as a key indicator for clinical evaluation of intestinal mucosal function [29]. IAP is a phosphatase mainly distributed in the intestinal brush border, which can regulate the balance of intestinal flora, inhibit endotoxin absorption, protect the intestinal mucosal barrier, and reduce inflammatory responses [30, 31]. AC is mainly secreted by the pancreas and salivary glands, and its core function is to break down starch into small-molecule carbohydrates to promote the digestion and absorption of carbohydrates [32]. GAS is a peptide hormone secreted by the duodenal mucosa and gastric antrum, which can promote gastric acid secretion; however, its excessive secretion can damage gastrointestinal function [33]. The results of this study showed that over time after IMV, the above-mentioned indicators in both groups showed a downward trend, with a more significant decrease in the early group. Specifically, at 48 h, the levels of GAS, DAO, and AC in the early group were significantly lower than those in the delayed group, while there was no significant difference in IAP between the two groups. At 72 h, the levels of GAS, DAO, IAP, and AC in the early group were all significantly lower than those in the delayed group. This suggests that early IMV can correct the hypoxic state in a timely manner in patients with SP complicated with gastrointestinal dysfunction, improve systemic tissue oxygen supply and gastrointestinal mucosal blood perfusion, and thereby achieve targeted repair of gastrointestinal function damage. On the one hand, it alleviates the ischemic-hypoxic injury of the gastrointestinal mucosa, inhibits the excessive secretion of GAS to reduce gastric acid-related gastrointestinal mucosal irritation, and also reduces the permeability of the intestinal mucosal barrier, decreasing the entry of DAO into the bloodstream to alleviate intestinal mucosal barrier dysfunction. On the other hand, after controlling pulmonary infection and systemic inflammatory response, the intestinal endotoxin load is reduced, allowing IAP to exert its protective effects of regulating flora and inhibiting endotoxin absorption more efficiently [34]. The changes in IAP levels also reflect the improvement of the intestinal inflammatory microenvironment. In addition, the reasonable decrease in AC levels suggests that early ventilation promotes the recovery of gastrointestinal digestive function and avoids the disorder of digestive enzyme secretion caused by persistent hypoxia [35].

The APACHE II score is commonly used for illness severity assessment in critically ill patients. The GIDS and CPIS are commonly used to evaluate gastrointestinal function and pulmonary infection, respectively. In this study, the above scale scores were selected, and the results showed that after IMV, the CPIS and GIDS scores in both groups decreased significantly at 48 h and 72 h, while the APACHE II score decreased only at 72 h. When comparing 72 h with 48 h after IMV, the APACHE II and GIDS scores in both groups decreased significantly, whereas the CPIS score decreased only in the early group. In terms of inter-group comparison, compared with the delayed group, the APACHE II and GIDS scores in the early group were significantly lower at both 48 h and 72 h, and the CPIS score was significantly lower only at 72 h. The above results indicate that early IMV is more conducive to improving patients' conditions. It can promptly correct hypoxia and reduce systemic inflammation, thereby more quickly alleviating the overall severity of critical illness (reflected by the decrease in APACHE II score) and repairing gastrointestinal function injury (reflected by the decrease in GIDS score). Although the improvement of pulmonary infec-

tion (reflected by the CPIS score) is slightly delayed, the effect in the later period is better [36]. In contrast, delayed ventilation lags behind in the control of illness condition, gastrointestinal function, and pulmonary infection, which further confirms the therapeutic value of early ventilation for this group of patients. Furthermore, in this study, the total adverse reaction rate in the early group (19.23%) was significantly lower than that in the delayed group (53.84%).

Several limitations still exist in this work. The small sample size of 52 cases in each group is prone to selection bias, and specific complications such as ventilator-associated lung injury and catheter-related infections were not monitored, resulting in insufficient evaluation dimensions. Mechanistically, early IMV promptly corrects hypoxia, inhibits systemic inflammation, and alleviates gastrointestinal mucosal ischemia, thereby reducing the risk of gastrointestinal symptoms such as nausea, diarrhea, and vomiting. Meanwhile, the rapid improvement of oxygenation can relieve dizziness and headache caused by cerebral hypoxia. In contrast, delayed ventilation leads to the persistence of inflammatory storms due to disease progression and more severe damage to the gastrointestinal barrier. Additionally, the accumulation of sedative drugs associated with prolonged IMV may further trigger diarrhea and exacerbate dizziness/headache, which collectively increase the incidence of adverse reactions. Future studies should be committed to conducting multicenter, large-sample prospective studies to validate these findings. Meanwhile, more dimensions of complications should be monitored and analyzed, and their underlying mechanisms should be explored in depth to provide a more solid evidence base for clinical decision-making.

In conclusion, for SP patients complicated with gastrointestinal dysfunction, implementing IMV within 6 h after the onset of IMV indications yields better therapeutic effects. It can reduce the body's inflammatory response, shorten the duration of IMV treatment and ICU stay, and improve blood gas indexes, thus demonstrating significant clinical application value.

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Disclosure of conflict of interest

None.

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