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Original Article

Effect of sivelestat on postoperative outcomes in patients with acute type A aortic dissection and hypoxemia: a retrospective analysis

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Abstract: Objectives: Preoperative hypoxemia in patients with acute type A aortic dissection (ATAAD) increases the risk of Postoperative pulmonary complications (PPCs). Sivelestat, which is used for acute lung injury has not been extensively studied in ATAAD patients who develop preoperative hypoxemia. This study first aims to evaluate the impact of sivelestat on the duration of postoperative mechanical ventilation and the length of stay in the Intensive Care Unit (ICU) for patients with ATAAD complicated by hypoxemia. Secondly, we investigate the effects of sodium sivelestat on the oxygenation index (OI, PaO_2/FiO_2) and serum inflammatory factors of patients. Methods: In this retrospective study, 143 patients diagnosed with ATAAD undergoing total aortic arch replacement with stent grafting (Sun's) at our hospital (2021-2024) were grouped into sivelestat and non-sivelestat groups. We obtained and compared patient data including demographics, hospitalization, ventilation, and perioperative biomarkers. Results: In total, 79 patients (55.2%) experienced preoperative hypoxemia based on the inclusion criteria. Eventually, 65 patients were enrolled in the study after excluding 14 patients. The postoperative PaO_2/FiO_2 decreased in both groups. The postoperative PaO_2/FiO_2 was significantly higher in the sivelestat group than in the non-sivelestat group at 3d (T2), 5d (T3), and 7d (T4). White blood cell count (WBCc) and neutrophil count (NEUTc) at T3 and T4, as well as a neutrophil percentage (NEUT%) at T4 in the sivelesta group were lower than that in the non-sivelestat group. Additionally, the C-reactive protein (CRP) and Interleukin-6(IL-6) levels in the sivelesta group at T3 and T4 were reduced. The mechanical ventilation duration, ICU, and hospital length of stay in the sivelesta group were shortened. Other clinical indices displayed no significant differences. Conclusion: In summary, patients with ATAAD and preoperative hypoxemia have lower postoperative PaO_2/FiO_2. Besides, sivelestat improves postoperative PaO_2/FiO_2, reduces inflammation, and shortens ventilation as well as ICU/hospital stay in ATAAD patients with preoperative hypoxemia.

Keywords: Sivelestat, hypoxemia, acute type A aortic dissection, oxygenation index, effect

Introduction

Acute type A aortic dissection (ATAAD) constitutes a surgical emergency necessitating immediate intervention. This condition occurs when an intimal tear permits blood entry into the aortic media, causing longitudinal separation of the intima to form a dissection flap that partitions the true lumen from the newly created false lumen. All dissections involving the ascending aorta, irrespective of the primary tear location, are classified as Stanford type A [1]. The International Registry of Acute Aortic Dissection (IRAD) further categorizes aortic dissections into four temporal phases: hyperacute (<24 h), acute (2-7 d), subacute (8-30 d), and chronic (>30 d) [2]. Although significant progress has been made in the development of medical treatments, the mortality rate of ATAAD is relatively high, ranging from 15-30% [3], largely attributable to high complication rates. Postoperative pulmonary complications (PPCs) contribute 30-50% of the ATAAD-related mortality and represent major prognostic determinants [4].

Notably, ATAAD patients with preoperative hypoxemia sshow reduced postoperative PaO_2/FiO_2 ratios and elevated risk of acute respiratory distress syndrome (ARDS), which is likely

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mediated by systemic inflammatory responses that induce alveolar-capillary membrane edema, thereby exacerbating pulmonary injury [5-7]. Furthermore, reperfusion injury during cardiopulmonary bypass (CPB) with deep hypothermic circulatory arrest (DHCA) triggers substantial inflammatory cytokine release and neutrophil activation, exacerbating secondary lung injury and leading to poor outcomes [8]. Therefore, it is imperative to initiate early therapies to alleviate postoperative hypoxemia and minimize systemic inflammatory response in ATAAD patients.

Sivelestat is a selective neutrophil elastase inhibitor that selectively attenuates neutrophil elastase-induced lung tissue damage and reduces inflammatory responses. It therefore improves postoperative PaO_2/FiO_2 and decreases the incidence of PPCs [9-11], resulting in enhanced early patient outcomes. In this study, we investigated the effects of sivelestat on postoperative PaO_2/FiO_2, serum inflammatory cytokines, duration of mechanical ventilation, and ICU stay in ATAAD patients with hypoxemia. The findings of this study are expected to provide evidence that will guide future clinical practice.

Materials and methods

Study population

After obtaining approval from the Ethics Committee of Beijing Anzhen Hospital Nanchong Branch, this retrospective analysis obtained data from 143 patients who underwent Sun's surgery at our institution between January 2021 and December 2024.

Inclusion criteria: ① Confirmed Stanford type A dissection per diagnostic standards; ② Preoperative PaO_2/FiO_2 <300 mmHg on arterial blood gas analysis; ③ Undergoing Sun's procedure within 48 hours of symptom onset. Patients meeting all above criteria were enrolled.

Exclusion criteria: ① Patients with preoperative diagnosed pulmonary infection, chronic obstructive pulmonary disease, cardiogenic pulmonary edema, or hepatic and renal insufficiency. ② Postoperative mortality. ③ Patients with severe hepatic and renal insufficiency postoperatively affecting civirestat metabolism. ④ Patients who developed postoperative sepsis/septic shock. ⑤ Patients with other diseases that may prolong postoperative ICU stay or hospitalization duration. ⑥ Patients with incomplete clinical data. Patients that met any of these criteria were excluded.

This study finally included a total of 65 patients. Depending on whether they received sivelestat treatment, the enrolled 65 patients were randomly assigned to either the sivelestat group or the non-sivelestat group. The sivelestat group, representing patients who received sivelestat treatment, and the non-sivelestat group, representing those who did not receive sivelestat treatment. The sivelesta group received sivelestat (National Medicine Approval Number H20203093, Shanghai Huirun Jiangsu Pharmaceutical Co., Ltd.).The 24-hour dose of sivelestat (4.8 mg·kg-1) was dissolved in normal saline, and drawn into a 50 mL syringe, adding to a total volume of 48 mL. The dose was administered intravenously using a micro-pump at a rate of 2 mL/h for a constant 24-hour infusion. Treatment was continued for 7 days in the sivelestat group, before evaluating the efficacy.

Surgical method and criteria for tube removal

All patients received the Sun's procedure with double cannulation of the femoral and axillary arteries. Following aortotomy, the aortic root repair was tailored based on intraoperative findings. The proximal ascending aorta was anastomosed to the trunk of the four-branched graft. When the nasopharyngeal temperature dropped to about 26.0°C, the circulation was stopped; unilateral selective cerebral perfusion was performed via the axillary artery; the decision for bilateral cerebral perfusion was based on the cerebral blood return from the left common carotid artery. The brachiocephalic trunk and left common carotid artery were transected, and a branch-type covered stent was implanted near the opening of the left common carotid artery. A 'sandwich' anastomosis was carried out between the artificial vessel, stent proximal end, and autologous vessel. The left common carotid artery and brachiocephalic trunk were sequentially anastomosed to the branches of the artificial vessel. The heart was restarted, gradually warmed, and fully vented. Hemodynamic stability was achieved at the anal temperature of ≥35°C; thus, the left heart drainage tube, atrial drainage tube, right axillary artery cannula, and femoral artery cannula were sequentially removed. A total of 143 patients were transferred to a cardiac specialized ICU for continued treatment after surgery and received tracheal intubation. The ventilator was weaned off once they met the following criteria for tracheal extubation: (1) clear consciousness, recovery of spontaneous breathing and limb muscle strength; (2) stable circulation and warm limbs; (3) postoperative drainage <50 ml/h, urine output reaching 1-2 ml/h/Kg; (4) stable internal environment.

Observational indicators

Preoperative Data: Age, sex, body mass index (BMI), hypertension, diabetes, coronary artery disease, pericardial effusion, shock, PaO_2/FiO_2. Laboratory indicators included WBCc, NEUTc, NEUT%, CRP, D-dimer (D-D), systolic blood pressure (SBP), diastolic blood pressure (DBP), ejection fraction (EF), creatinine, cystatin-C (Cys-C), aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

Intraoperative Data: Operative time, aortic cross-clamp time, cardiopulmonary bypass time, deep hypothermic circulatory arrest time, intraoperative blood usage, and concomitant surgeries. Postoperative Data: hospital stay, ICU length of stay, duration of mechanical ventilation, Incidence of unplanned reintubation, Tracheostomy requirement rate, Non-invasive ventilation utilization rate. Laboratory indicators included PaO_2/FiO_2, WBCc, NEUTc, NEUT%, CRP, IL-6, procalcitonin (PCT), B-type natriuretic peptide (BNP),creatinine (Cr), AST, ALT at postoperatively 2 hours (T0), 1 day (T1), 3 days (T2), 5 days (T3), and 7 days (T4). This study performs a comparative analysis of the following postoperative parameters between the two groups, including: Hospital stay, ICU length of stay, Duration of mechanical ventilation, Incidence of unplanned reintubation, Tracheostomy requirement rate, Non-invasive ventila-tion utilization rate,PaO_2/FiO_2, WBCc, NEUTc, NEUT%, CRP, IL-6. Primary objective: To determine intergroup differences in these metrics and assess the impact of sivelestat on postoperative outcomes in patients undergoing acute type A aortic dissection repair with concomitant hypoxemia.

Statistical analysis

Data analysis was performed using SPSS 27.0 software. Continuous variables were presented as the mean ± standard deviation. Variables including PaO_2/FiO_2, WBCc, NEUTc, NEUT%, CRP, and IL-6, were analyzed by the independent samples t-test or paired samples t-test. Categorical variables were expressed as frequencies (n, %). Parameters such as, hospital stay, ICU length of stay, duration of mechanical ventilation, incidence of unplanned reintubation, tracheostomy requirement rate, and noninvasive ventilation utilization rate, were analyzed using the Chi-square test or corrected Chi-square test, or Fisher's exact test. Statistical significance was set at $P<0.05$.

Results

Comparison of preoperative general data and laboratory indicators

A total of 79 patients (55.2%) developed preoperative hypoxemia and enrolled in the study based on the inclusion criteria. Among them, 65 patients (30 patients in the sivelestat group and 35 patients in the non-sivelestat group) were included in the study, while 14 patients were excluded (**Figure 1**). No significant differences were observed between the two groups in terms of gender, age, BMI, hypertension, diabetes, coronary artery disease (CAD), shock, pericardial effusion, SBP, DBP, EF, and preoperative laboratory indexes including PaO_2/FiO_2, WBCc, NEUTc, NEUT%, CRP, IL-6, D-D, Cr, Cys-C, AST, ALT ($P>0.05$) (**Table 1**).

Comparison of intraoperative indicators

The analysis revealed significant differences between the two groups in intraoperative indicators, such as operative time, aortic cross-clamp time, cardiopulmonary bypass time, deep hypothermic circulatory arrest time, intraoperative blood usage, and concomitant surgeries ($P>0.05$) (**Table 2**).

Postoperative parameter comparison

Comparison of PaO_2/FiO_2: In both groups, postoperative PaO_2/FiO_2 was significantly lower than preoperative values ($P<0.05$), and the number of patients experiencing moderate to severe hypoxemia was higher postoperatively ($P<0.05$) (**Table 3**). Notably, treatment with Sivelestat increased the PaO_2/FiO_2 (**Figure 2**) at T2, T3, and T4 compared to the non-sivelestat group ($P<0.05$), but there was no significant difference at T1 and T2 ($P>0.05$).

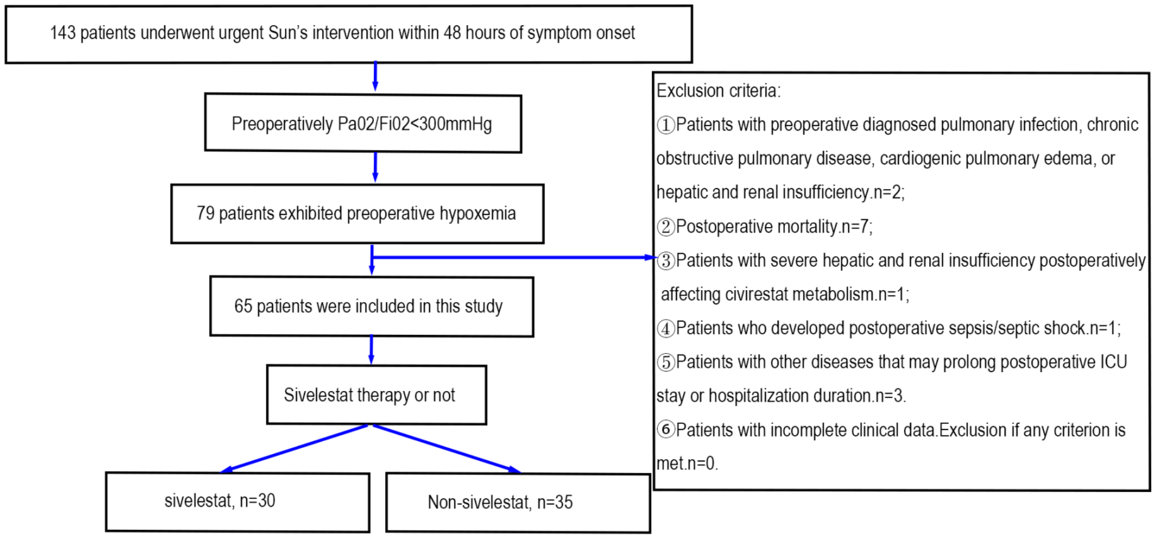

Figure 1. Flow chart of study population selection. Note: PaO_2/FiO_2: oxygenation index; n: number; ICU: Intensive Care Unit.

Table 1. Clinical characteristics and preoperative data of sivelestat group and non-sivelestat group

	N (n=35)	S (n=30)	P
Age (y)	57.80±12.59	57.50±12.03	0.92
Gender (male/female)	23/12	19/11	0.84
BMI (Kg/m^2)	27.13±3.60	27.17±2.63	0.97
Hypertension, n (%)	32 (91.4)	28 (93.3)	1.00
Diabetes, n (%)	3 (8.6)	3 (10)	1.00
CAD, n (%)	3 (8.6)	4 (13.3)	0.83
Shock, n (%)	2 (5.7)	4 (13.3)	0.53
pericardial effusion, n (%)	19 (54.3)	16 (53.3)	0.94
SBP (mmHg)	138.00±28.33	143.40±32.47	0.48
DBP (mmHg)	79.86±19.05	85.33±20.17	0.27
EF (%)	60.34±4.92	62.63±5.44	0.08
PaO_2/FiO_2 (mmHg)	253.08±36.12	254.04±32.12	0.91
WBCc (10^3/ml)	13.02±3.98	12.74±4.06	0.78
NEUTc (10^3/ml)	11.23±3.67	10.96±3.91	0.77
NEUT%			
CRP (mg/L)	32.72±57.49	28.59±49.60	0.76
D-Dimer (ug)	86.01±164.70	33.80±47.09	0.10
Cr (mmol/L)	93.33±49.97	90.17±49.37	0.80
Cys-C (mg/L)	1.33±0.99	1.30±1.13	0.91
AST (U/L)	43.07±67.71	36.3±49.03	0.630
ALT (U/L)	27.36±33.31	39.35±69.64	0.394

Note: BMI: body mass index; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; EF: ejection fraction; PaO_2/FiO_2: oxygenation index; WBCc: white blood cell count; NEUTc: neutrophil count; NEUT%: neutrophil percentage; CRP: C-reactive protein; Cr: creatinine; Cys-C: cystatin-C; AST: aspartate aminotransferase; ALT: alanine aminotransferase; y: year; n: number.

Comparison of WBCc, NEUTc, and NEUT%: The levels of WBCc, NEUTc, and NEUT% at T0, T1, and T2 were comparable between the two groups. However, the sivelestat group exhibited lower WBCc and NEUTc (**Figure 3A**) at T3 and T4, as well as lower NEUT% (**Figure 3B**) at T4 ($P<0.05$) relative to the non-sivelestat group.

Comparison of CRP and IL-6: Analysis of CRP and IL-6 at various times between the two groups showed that the sivelestat group had lower CRP (**Figure 4A**) and IL-6 (**Figure 4B**) levels at T3 and T4 compared to the non-sivelestat group ($P<0.05$). However, no significant differences were observed in CRP and IL-6 levels at T1 and T2 ($P>0.05$). Furthermore, PCT, Cr, BNP, AST, ALT, and other parameters were not significantly different between the two groups ($P>0.05$) at all postoperative time points (**Table 4**).

Comparison of ventilator duration, ICU, and hospital length of stay: The ICU and hospital length of stay (**Figure 5A**), and ventilation duration (**Figure 5B**) were lower in the sivelestat group compared to the non-sivelestat group ($P<0.05$). The

Table 2. Intraoperative data of the sivelestat group and non-sivelestat group

	N (n=35)	S (n=30)	P
operative time (min)	435.86±69.28	430.70±54.10	0.74
aortic cross-clamp time (min)	132.37±17.41	131.07±20.80	0.79
CPB (min)	211.29±36.61	200.37±30.21	0.19
DHCA (min)	24.09±5.35	26.07±4.31	0.10
intraoperative blood usage (ml)	2075.43±1150.45	2444.33±627.75	0.12
concomitant surgeries			
Bentall, n (%)	8 (22.86)	10 (33.33)	0.35
Aortic ascending replacement, n (%)	22 (62.86)	18 (60)	0.81
David, n (%)	3 (8.57)	1 (3.33)	0.72
Carbrol, n (%)	1 (2.86)	1 (3.33)	1.00
Wheat, n (%)	1 (2.86)	0 (0)	1.00

Note: CPB: cardiopulmonary bypass time; DHCA: deep hypothermic circulatory arrest time; n: number.

Table 3. The data of pre-and postoperative PaO_2/FiO_2 and severity in the sivelestat group and non-sivelestat group

	pre-operation (n=65)	post-operation (n=65)	P
PaO_2/FiO_2 (mmHg)	253.5±34.07	197.57±66.50	<0.001
Severity of Hypoxemia	n (%)	n (%)	
Mild	62 (95.38)	31 (47.69)	<0.001
Moderate	3 (4.62)	27 (41.54)	<0.001
Severe	0 (0)	7 (10.77)	0.007

Note: PaO_2/FiO_2: oxygenation index; n: number.

non-sivelestat group had higher rates of postoperative reintubation or tracheostomy (11.4%) and non-invasive ventilation usage (31.4%) compared with the sivelestat group (3.3% and 20.0%, respectively). However, these differences were not significant (P>0.05) (**Table 4**). Unplanned re-intubation or tracheotomy rate (%) = the number of patients requiring unplanned reintubation and tracheostomy/N×100; Non-invasive ventilation usage rate (%) = the number of patients requiring non-Invasive ventilation/N×100; N (The non-sivelestat group) =35, N (The sivelestat group) =30.

Discussion

Hypoxemia is one of the most common perioperative complications in patients with ATAAD. It is characterized by a PaO_2/FiO_2 of <300 mmHg [12]. Preoperative hypoxemia is an independent risk factor for postoperative hypoxemia or ARDS [6, 13], which increases the postoperative mortality in patients with ATAAD. The prevalence of preoperative hypoxemia in ATAAD patients varies between 41.5% and 78.5%, and there is no standard diagnostic criteria [4, 14, 15]. This study enrolled ATAAD patients with a preoperative PaO_2/FiO_2 of <300 mmHg; and found that 55.2% developed preoperative hypoxemia.

Clinically, the severity of hypoxemia is evaluated using the PaO_2/FiO_2. According to the Berlin definition, hypoxemia is categorized into three classes, including mild (PaO_2/FiO_2 range of 200-300 mmHg), moderate (range of 100-200 mmHg), and severe (PaO_2/FiO_2 <100 mmHg) [16]. Due to the effect of excessive inflammatory response, most patients with ATAAD presented with preoperative hypoxemia. These patients, subjected to intraoperative factors including massive blood transfusion, CPB, and DHCA, are at risk of further pulmonary injury, further causing a reduction in PaO_2/FiO_2 [17, 18]. The findings showed that, in contrast to preoperative values, postoperative PaO_2/FiO_2 ratios were significantly decreased in both groups, indicating a worsening of hypoxemia. These results suggest that cardiopulmonary bypass combined with deep hypothermic circulatory arrest further aggravates pulmonary injury in patients following surgery.

Of note, pharmacological intervention is recommended for patients developing hypoxemia. This has conventionally included ulinastatin [19], sevoflurane [20], and NO [21], which primarily suppress inflammatory responses or improve lung injury. Sivelestat is a novel inter-

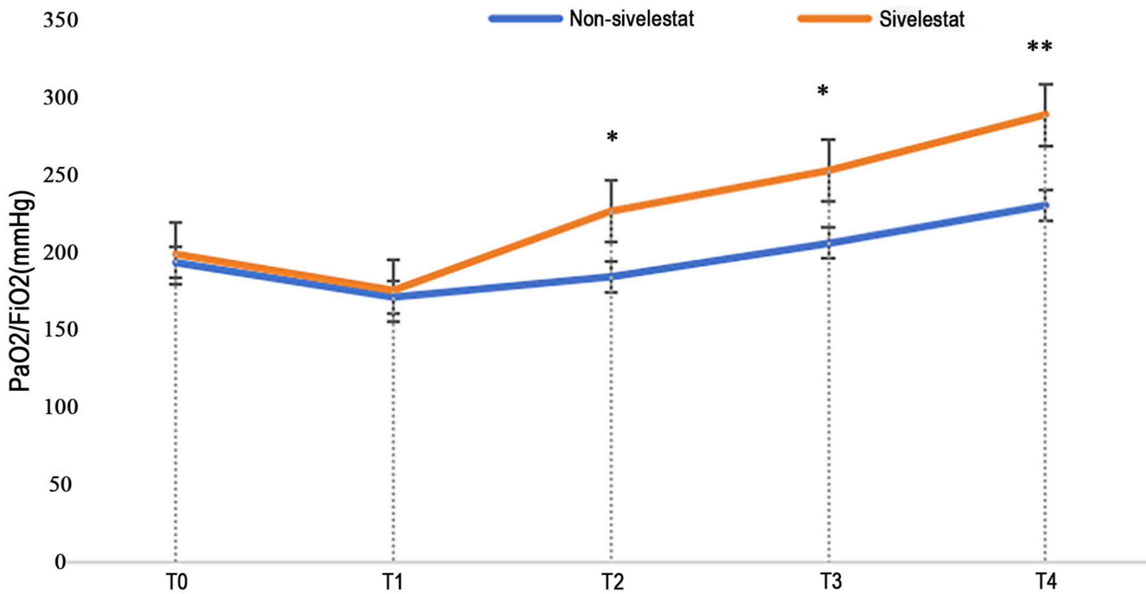

Figure 2. Line chart of postoperative PaO_2/FiO_2 in two patient groups. Note: PaO_2/FiO_2: oxygenation index; T0: postoperatively 2 hours; T1: postoperatively 1 day; T2: postoperatively 3 days; T3: postoperatively 5 days; T4: postoperatively7 days. *: P<0.05; **: P<0.01.

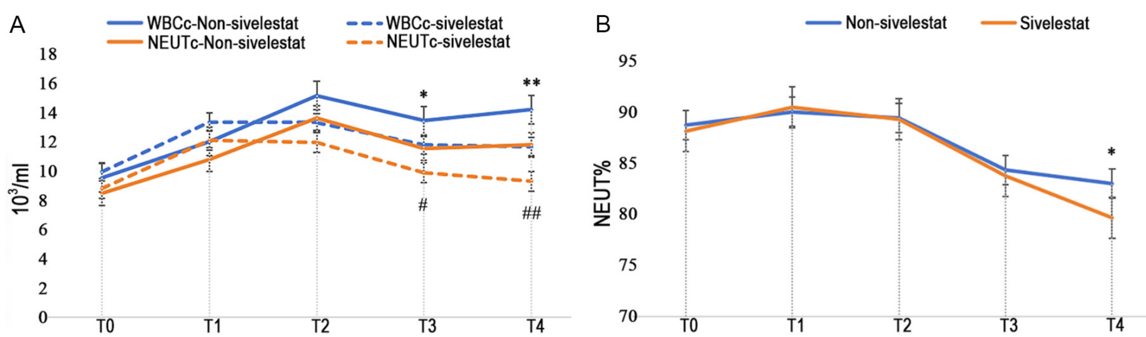

Figure 3. Line chart of postoperative WBCc, NEUTc, and NEUT% in two patient groups. Note: *Comparison of WBCc between the two groups; #Comparison of NEUTc between the two groups; NEUT%: neutrophil percentage; T0: postoperatively 2 hours; T1: postoperatively 1 day; T2: postoperatively 3 days; T3: postoperatively 5 days; T4: postoperatively7 days. *: P<0.05; **: P<0.01; #: P<0.05; ##: P<0.01.

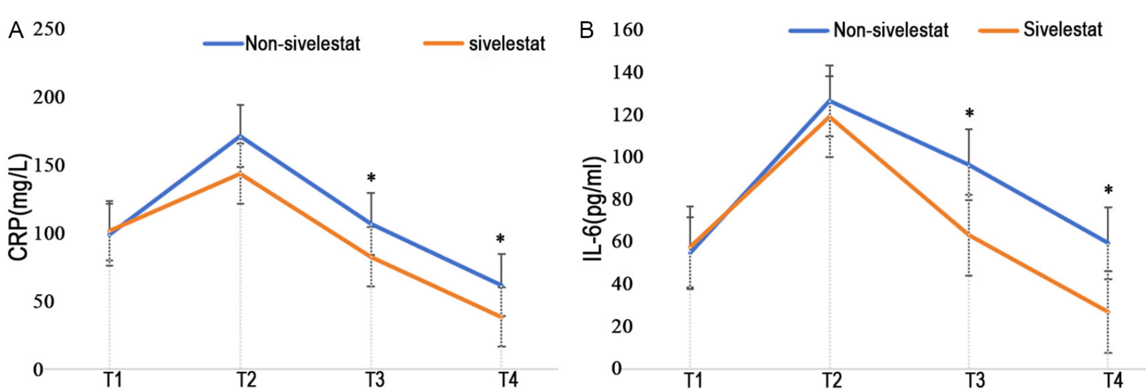

Figure 4. Line chart of postoperative CRP and IL-6 in two patient groups. Note: CRP: C-reactive protein; IL-6: Interleukin-6; T0: postoperatively 2 hours; T1: postoperatively 1 day; T2: postoperatively 3 days; T3: postoperatively 5 days; T4: postoperatively7 days. *: P<0.05.

Table 4. Post-operative data of the sivelestat group and non-sivelestat group

	Non-sivelestat (n=35)	Sivelestat (n=30)	P
Re-intubation or tracheostomy, n (%)	4 (11.4)	1 (3.3)	0.45
Non-invasive ventilation, n (%)	11 (31.4)	6 (20)	0.30
PCT (ng/ml)			
T1	6.34±6.76	6.78±6.53	0.79
T2	4.82±3.39	4.84±4.15	0.99
T3	3.19±3.20	2.43±2.03	0.27
T4	1.95±1.96	1.59±1.50	0.41
BNP (pg/ml)			
T1	2513.56±2513.86	2473.37±1510.37	0.93
T2	3792.88±2262.64	3720.60±2066.43	0.89
T3	3925.90±2402.60	3661.37±2146.79	0.64
T4	2775.08±2258.23	2128.37±1179.68	0.16
Cr (mmol/L)			
T0	106.52±36.03	98.65±41.60	0.42
T1	129.44±48.77	124.07±52.27	0.67
T2	111.76±34.53	126.01±57.88	0.24
T3	91.64±23.81	101.27±44.83	0.27
T4	83.11±26.05	85.97±35.13	0.71
AST (U/L)			
T0	63.77±37.15	52.88±24.63	0.18
T1	83.97±75.85	73.22±70.67	0.56
T2	60.86±41.80	51.97±41.07	0.39
T3	54.81±61.16	46.99±34.56	0.54
T4	41.70±28.41	42.76±42.12	0.91
ALT (U/L)			
T0	28.20±21.23	23.66±14.37	0.31
T1	41.35±51.30	28.47±24.30	0.19
T2	50.04±61.62	37.83±44.81	0.37
T3	52.93±54.05	41.74±31.55	0.32
T4	47.75±43.63	42.30±33.33	0.58

Note: PCT: procalcitonin; BNP: B-type natriuretic peptide; Cr: creatinine; AST: aspartate aminotransferase; ALT: alanine aminotransferase; T0: postoperatively 2 hours; T1: postoperatively 1 day; T2: postoperatively 3 days; T3: postoperatively 5 days; T4: postoperatively7 days. n: number.

vention drug that exerts lung-protective effects via multiple pathways. It was marketed in Japan in 2002 and approved for use in patients with ALI/ARDS associated with systemic inflammatory response syndrome (SIRS). During the COVID-19 pandemic in 2020, sivelestat was extensively used to treat ARDS [22-24]. As a selective inhibitor of neutrophil elastase, sivelestat prevents lung tissue damage caused by neutrophil elastase [25-27] and exerts lung-protective effects by suppressing signaling pathways including transcription activator proteins or the tumor necrosis factor-α (TNF-α) pathway [28, 29]. Herein, we discovered that patients in the sivelestat group had a higher PaO_2/FiO_2 than those in the non-sivelestat group. This demonstrates that sivelestat can improve postoperative oxygenation levels and lung function in ATAAD patients with hypoxemia.

Studies have shown that inflammatory responses are prevalent during the perioperative period in ATAAD patients, which is driven by various types of serine proteases. For instance, neutrophils induce enzymes including human neutrophil elastase (hNE) [30]. Notably, hNE is a serine protease released by neutrophils during inflammation [31, 32] and modulates the pathophysiology of various diseases, particularly

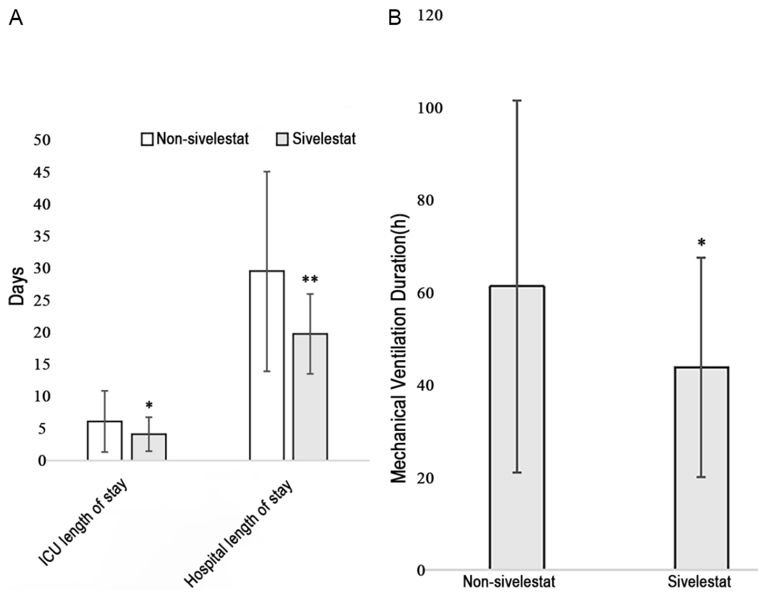

Figure 5. Bar graph of ventilator duration, ICU, and hospital length of stay in two patient groups. Note: T0: postoperatively 2 hours; T1: postoperatively 1 day; T2: postoperatively 3 days; T3: postoperatively 5 days; T4: postoperatively 7 days; *: P<0.05; **: P<0.01.

inflammatory lung conditions. hNE directly activates inflammation by increasing the expression and release of cytokines and indirectly activates inflammation by causing a release of extracellular traps and exosomes, hence amplifying protease activity and the inflammatory response in the airways [33, 34], as well as exacerbating lung injury.

Sivelestat is a synthetic, specific low-molecular-weight inhibitor of neutrophil elastase that effectively inhibits inflammatory cytokines produced by pulmonary epithelial and endothelial cells [35, 36], thereby reducing cytokine-induced neutrophil release of elastase and breaking the vicious cycle of lung injury mechanisms. This work revealed that after sivelestat treatment, patients had lower levels of WBCc, NEUTc, NEUT%, CRP, and IL-6 in the sivelestat group than in the non-sivelestat group. This shows that sivelestat can suppress the expression of inflammatory factors and alleviate pulmonary inflammatory responses. However, the study was based on a small sample size; although there was a statistical significance for the primary outcome, it was likely underpowered for secondary outcomes such as biomarker analysis.

Furthermore, this study demonstrates that sivelestat-treated patients exhibited significantly reduced clinical time metrics compared to the non-sivelestat group: ICU length of stay (P<0.05), hospital length of stay (P<0.01), and mechanical ventilation duration (P<0.05). Sivelestat is a selective, reversible, competitive neutrophil elastase inhibitor reported to exert anti-inflammatory and lung-protective effects through multiple pathways, reducing postoperative ventilation duration, ICU length of stay, and hospital length of stay [37, 38], this study further empirically confirms this mechanistic perspective.

Notably, these findings are consistent with our observations. However, the differences in re-intubation or tracheostomy rates (11.4% vs 3.3%, P=0.45) and non-invasive ventilation usage rates (31.4% vs 20.0%, P=0.30) were not significant (11.4% vs 3.3%, P=0.45). However, post hoc power analysis revealed that the statistical power to detect an 8.1% difference was only 21.9%, confirming the risk of a Type II error (β error). Therefore, the possibility of clinically relevant differences cannot be ruled out.

In conclusion, sivelestat improves the postoperative PaO_2/FiO_2 in patients with ATAAD and hypoxemia, attenuates inflammatory cytokines, and reduces postoperative ventilation duration, ICU, and Hospital Length of Stay (**Figure 6**).

Limitations

This study has limitations. First, it is a single-center retrospective analysis, which inherently limits the generalizability of its conclusions. Secondly, the study used a small sample size; despite being statistically significant, the study is likely underpowered for secondary outcomes like biomarker comparisons. The findings should be validated in larger patient cohorts. Moreover, the short observation period introduces a potential bias risk, which must be considered when interpreting the results. We also adopted a specific definition of hypoxemia, which limits the scope of our findings. Lastly, the retrospective design of the study restricted the measurement of other markers including

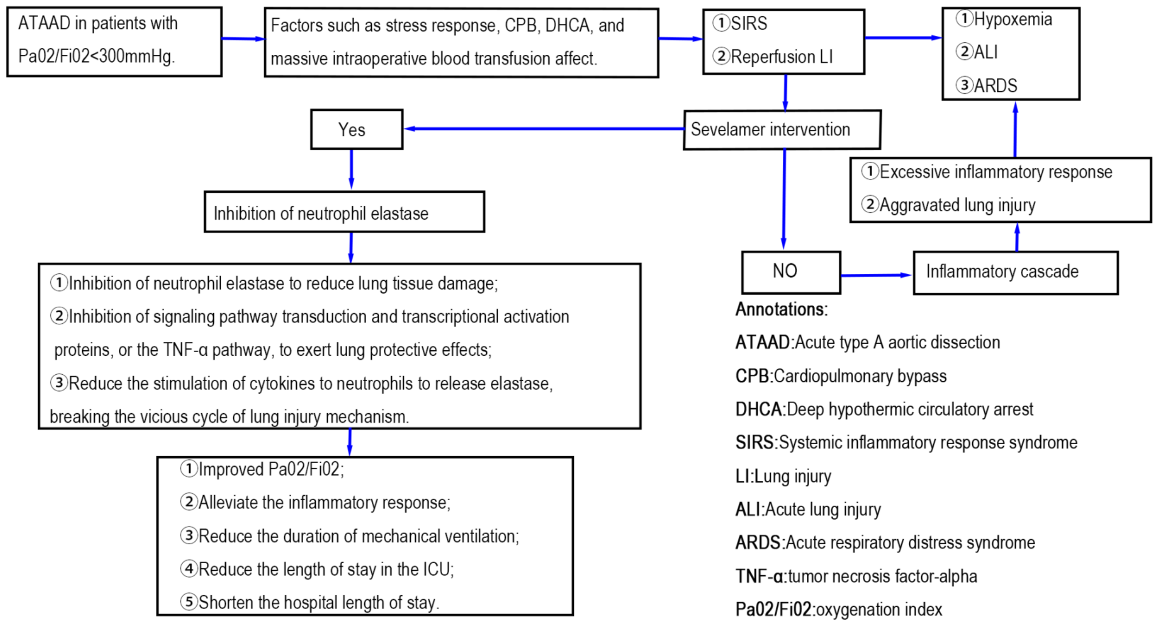

Figure 6. Flow chart of study summary. Note: ATAAD: Acute type A aortic dissection; CPB: Cardiopulmonary bypass; DHCA: Deep hypothermic circulatory arrest; SIRS: Systemic inflammatory response syndrome; LI: Lung injury; ALI: Acute lung injury; ARDS: Acute respiratory distress syndrome; TNF-α: tumor necrosis factor-alpha; Pa02/Fi02: oxygenation index.

IL-1, IL-8, and TNF-α that could help in understanding PIS.

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All patients provided written consent for data collection.

Disclosure of conflict of interest

None.

Abbreviations

ATAAD, Acute type A aortic dissection; IRAD, International Registry of Acute Aortic Dissection; PPCs, Postoperative pulmonary complications; ICU, Intensive Care Unit; PaO_2/FiO_2, Oxygenation index; WBCc, White blood cell count; NEUTc, Neutrophil count; NEUT%, Neutrophil percentage; CRP, C-reactive protein; IL-6, Interleukin-6; ARDS, Acute respiratory distress syndrome; CPB, Cardiopulmonary bypass; DHCA, Deep hypothermic circulatory arrest; D-D, D-dimer; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; EF, Ejection fraction; Cys-C, Cystatin-C; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; PCT, Procalcitonin; BNP, B-type natriuretic peptide; Cr, Creatinine; BMI, Body mass index; CAD, Coronary artery disease; SIRS, Systemic inflammatory response syndrome; TNF-α, Tumor necrosis factor-α; hNE, Human neutrophil elastase.

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