Predicting the Occurrence of Oxygenation Impairment in Patients with Type-B Acute Aortic Dissection

Kazunori Tomita, MD[1] Noritake Hata, MD, PhD[1] Nobuaki Kobayashi, MD, PhD[1] Takuro Shinada, MD, PhD[1] Akihiro Shirakabe, MD, PhD[1]

[1] Intensive Care Unit, Chiba Hokusoh Hospital, Nippon Medical School, Chiba, Japan

Address for correspondence Noritake Hata, MD, PhD, Intensive Care Unit, Chiba Hokusoh Hospital, Nippon Medical School, 1715 Kamagari, Inzai, Chiba, Japan 270-1694 (e-mail: hata-n@nms.ac.jp).

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Abstract

Complicated respiratory failure requiring mechanical ventilation in patients with type-B acute aortic dissection (AAD) has been previously reported, and inflammatory reactions have been found to be associated with the occurrence of oxygenation impairment (OI). However, the possibility of predicting the occurrence of OI in patients with type-B AAD has not yet been evaluated. This study was performed to investigate the possibility of predicting the occurrence of OI in type-B AAD. In this study, 79 type-B AAD patients were enrolled to investigate the possibility of predicting the occurrence of OI. OI was defined as $P_{O_2}/F_{IO_2} \leq 200$. Patient characteristics, type of AAD, vital signs on admission, and the presence of inflammatory reactions obtained on admission day were evaluated. OI occurred in 39 patients (49%) on hospital day 2.5 $\pm$ 1.4 on average. Younger age, male gender, nonslender frame (body mass index $\geq$ 22 kg/m^2), a relatively high maximum body temperature on the admission day ($\geq$ 36.5°C), DeBakey IIIb type, patent false lumen, and lower P_{O_2}/F_{IO_2} on admission were found to be associated with the occurrence of OI. Multivariate analysis revealed that nonslender frame, relatively high body temperature on the admission day, and lower P_{O_2}/F_{IO_2} on admission were reliable for predicting the occurrence of oxygen impairment. The occurrence of OI in type-B AAD can be predicted in the clinical setting.

Keywords
- acute aortic dissection
- inflammation
- oxygenation impairment
- prediction

Acute aortic dissection (ADD) is a life-threatening cardiovascular disease that is frequently complicated by systemic disorders. The outcomes of patients with type-B AAD[1] are better than those of patients with type-A AAD,[2–4] although multiple organ failure, including respiratory failure requiring mechanical ventilation, has been reported.[5–10] Although previous investigators have reported that oxygenation impairment (OI) is associated with systemic inflammatory reactions and distension of aortic dissections,[5,6,10–13] the possibility of predicting the occurrence of OI in patients with type-B AAD has not been investigated because they stated that there was relationship between OI and peak values of inflammation during hospitalization. Therefore, we retrospectively evaluated factors associated with the occurrence of OI in type-B AAD patients and investigated the possibility of predicting the occurrence of OI during the acute phase of AAD for the prevention and management of respiratory distress.

Method

This study was conducted in accordance with the ethical standards of the Declaration of Helsinki, and the Institutional Ethics Review Board (Ethics Review Board of Chiba Hokusoh Hospital, Nippon Medical School) approved the study protocol (approval number 319). All data were retrospectively collected from medical records. Therefore, written informed consent was not required by the ethics review board, and the

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concept of the study was disclosed on a poster displayed in the institute. No financial support was received for this study, and there are no conflicts of interest to declare.

Study Population

In this study, 93 consecutive patients with type-B AAD admitted to the intensive care unit of the university hospital between January 2000 and November 2011 were enrolled. Eight patients were excluded due to emergency surgery, late admission (more than 24 hours after the onset of symptoms), or inadequate medical records. Patients with OI due to pneumonia (five patients) and heart failure (one patient) were also excluded. Therefore, the final study population included 79 type-B AAD patients (mean age: 66.8 ± 12.9 years, 52 males and 27 females).

Evaluation of Clinical Findings and Diagnosis

Data regarding patient backgrounds, clinical findings, and in-hospital outcomes were retrospectively collected from the patients' medical records. The patient background data included age, gender, body height, body weight, body mass index, past medical history and habit, and the time from the onset of symptom to hospital admission. Vital signs (blood pressure, heart rate, and body temperature) and laboratory findings, including white blood cell (WBC) counts, the serum C-reactive protein (CRP) and creatinine levels, and findings of arterial blood gas analyses, obtained during intensive care were investigated. The arterial blood gas levels were measured using an automatic blood gas analyzer system (ABL 700, Radiometer, Copenhagen, Denmark). The oxygenation index was calculated according to the P_{O_2}/F_{IO_2} ratio (P/F ratio), and the estimated F_{IO_2} level was adopted as the F_{IO_2} value in patients not receiving mechanical ventilation support.[14] OI was defined as a P/F ratio ≤ 200 during intensive management.[15] In addition, the study patients were divided into two groups: those with (OI group) and those without (non-OI group) OI during intensive care.

The diagnosis of type-B AAD was made based on the results of contrast medium-enhanced computed tomography (CT). The type of AAD was classified according to the degree of involvement of the abdominal aorta (DeBakey IIIa or IIIb)[16] and the presence of thrombosed false lumens or patent false lumens, including partial thrombosis.[17]

Factors affecting the occurrence of OI were evaluated, and findings obtained on the admission day were used as predictive factors.

Statistical Analysis

All continuous data are expressed as the mean ± standard deviation, and mean differences between groups were analyzed using Student *t*-test. Proportional differences were analyzed using Fisher exact test. Categorical variables were analyzed using χ^2 test. A univariate analysis was used to evaluate factors predicting the occurrence of OI. In addition, cutoff values for factors associated with the occurrence of OI and prediction scores were calculated from receiver operating characteristic (ROC) curves. A multivariate logistic regression model was also used to evaluate factors associated with the occurrence of OI. A p value < 0.05 was considered to be statistically significant. All data were analyzed using the StatView 5 software package for Windows (SAS Institute, Cary, NC) and SPSS 14.0 J for Windows (SPSS Japan Institute, Tokyo, Japan).

Results

OI occurred in 39 of 79 type-B AAD patients (49.4%) on hospital day 2.5 ± 1.4 on average (►**Fig. 1**).

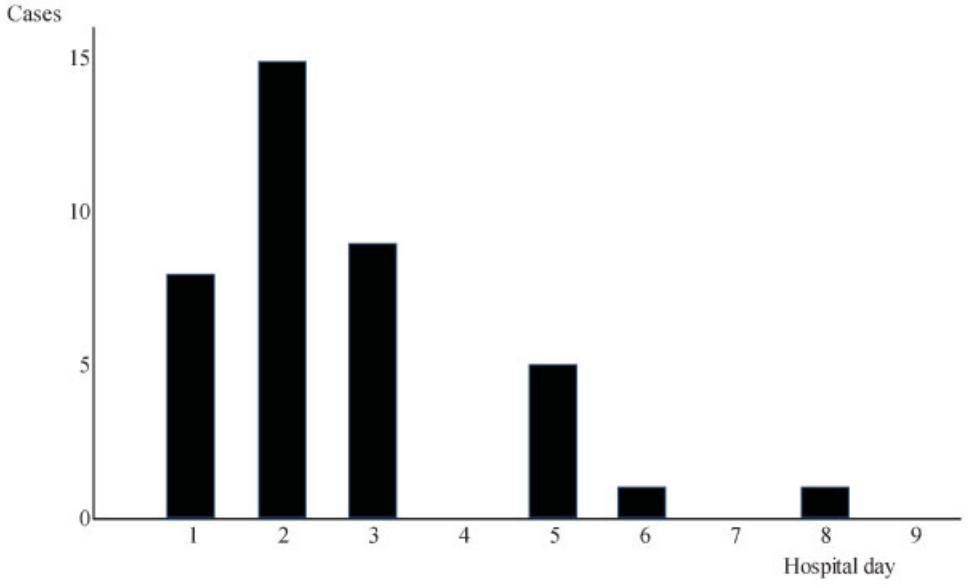


Fig. 1 Occurrence of oxygenation impairment after the onset of type-B acute aortic dissection.

Table 1 Background of patients and clinical findings on admission

	Total	OI group	Non-OI group	*p* value
	n = 79	*n* = 39	*n* = 40	
Age (years)	66.8 ± 12.9	63.6 ± 12.7	69.9 ± 12.4	0.0281
Gender (male/female)	52/27	30/9	22/18	0.0135
Medical history				
Hypertension (yes/no)	72/7	37/2	35/5	0.2490
Diabetes mellitus (yes/no)	6/73	3/36	3/37	0.9743
Dyslipidemia (yes/no)	29/50	17/22	12/28	0.2103
COPD (yes/no)	4/75	2/37	2/38	0.9793
Smoking (yes/no)	58/21	32/7	26/14	0.0863
Body mass index	24.3 ± 4.0	25.6 ± 4.0	23.0 ± 3.6	0.0025
Vital signs on admission				
Systolic blood pressure (mm Hg)	175.0 ± 34.4	181.5 ± 29.7	168.6 ± 37.8	0.0953
Diastolic blood pressure (mm Hg)	92.0 ± 19.9	95.6 ± 20.2	88.4 ± 19.2	0.1052
Body temperature (°C)	36.2 ± 0.6	36.2 ± 0.7	36.2 ± 0.6	0.5535
Time from onset to admission (hours)	3.2 ± 3.8	2.7 ± 3.7	3.7 ± 3.9	0.2056
Serum creatinine (mg/dL)	0.96 ± 0.43	0.94 ± 0.46	0.98 ± 0.42	0.6863
Po_2/Fio_2 on admission	305.2 ± 97.7	253.5 ± 85.4	355.6 ± 81.9	< 0.0001
Type of aortic dissection				
DeBakey (IIIa/IIIb)	13/66	3/36	10/30	0.0381
False lumen (thrombosed/patent)	47/32	18/21	29/11	0.0171

Abbreviations: COPD, chronic obstructive pulmonary disease; OI, oxygenation impairment.

Patients' Backgrounds and Types of AAD

The backgrounds of the patients and the clinical findings obtained on admission, including the type of AAD (DeBakey classification and the patency of false lumens), are shown in ►**Table 1**. The patients in the OI group were younger (63.6 ± 12.7 years), larger body mass index (24.3 ± 4.0 kg/m^2) and included more males (30 males, 77%) than the patients in the non-OI group (69.9 ± 12.4 years; body mass index: 23.0 ± 3.6 kg/m^2; 22 males, 55%).

AAD type DeBakey IIIb (92.3%) and the presence of patent false lumens (53.8%) were more frequently seen in the OI group than non-OI group (75.0 and 27.5%, respectively). However, there were no differences in vital signs on admission and the time from the onset of symptom to hospital admission between the two groups. No patient fell to shock vital requiring additional treatment after admission. P/F ratio on admission was significantly lower in the OI group (253.5 ± 85.4) than non-OI group (355.6 ± 81.9).

Oxygenation Impairment and Inflammatory Reactions

The inflammatory factors affecting the occurrence of OI in the type-B AAD patients during intensive care are shown in ►**Table 2**. The WBC counts after hospital day 2 and the serum levels of CRP after hospital day 3 were higher in the OI group, however, there were no differences on the admission day. Furthermore, the maximum body temperature was higher in the OI group than non-OI group only on the admission day. OI was found on admission in six patients, in whom only the WBC count was less (6,557 ± 3,594/μL) than those without OI on admission (9,881 ± 2,925/μL).

Predicting the Occurrence of Oxygenation Impairment

As OI occurred on hospital day 2.5 on average, seven factors obtained on admission day (younger age, male gender, nonslender frame, DeBakey IIIb, patent false lumen, relatively high maximum body temperature on the admission day, and low P/F ratio on admission) were investigated for their ability to predict the occurrence of OI after the onset of type-B AAD. The cutoff levels were determined using ROC curves according to age (< 68 years), nonslender frame (BMI ≥ 22 kg/m^2), relatively high maximum body temperature on the admission day (> 36.5°C), and low P/F ratio on admission (< 300). These seven factors were found to be significantly associated with the occurrence of OI in a univariate analysis (►**Table 3**). Using a multivariate logistic regression model, nonslender frame, relatively high maximum body temperature on the admission day, and low P/F ratio on admission were found to be independently associated with the occurrence of OI (►**Table 4**).

►**Fig. 2** demonstrates the predictive power for the occurrence of OI after AAD. The scores, defined as the number of applicable factors, including nonslender frame (BMI ≥ 22 kg/m^2), relatively high maximum body temperature on the admission day (> 36.5°C), and lower P/F ratio on admission (< 300), were able to predict the occurrence of OI when the

Table 2 Inflammatory reactions

	OI group	Non-OI group	*p* value
	n = 39	*n* = 40	
WBC (/μL)			
Day 1	9,788 ± 3,290	9,472 ± 2,902	0.6510
Day 2	11,674 ± 3,040	8,966 ± 2,568	< 0.0001
Day 3	11,481 ± 3,009	9,210 ± 2,438	0.0004
Day 4	10,706 ± 2,895	8,786 ± 2,091	0.0014
Day 5	9,328 ± 2,141	8,088 ± 2,211	0.0201
Maximum	12,865 ± 2,934	10,785 ± 3,382	0.0046
CRP (mg/dL)			
Day 1	0.50 ± 1.04	0.42 ± 0.67	0.6734
Day 2	3.77 ± 3.18	3.00 ± 2.35	0.2252
Day 3	12.33 ± 4.21	9.22 ± 4.26	0.0017
Day 4	15.29 ± 6.08	11.22 ± 5.72	0.0036
Day 5	14.46 ± 7.30	9.61 ± 5.61	0.0029
Maximum	17.07 ± 7.18	12.97 ± 5.96	0.0071
Maximum BT of the day (°C)			
Day 1	36.9 ± 0.7	36.5 ± 0.7	0.0261
Day 2	37.6 ± 0.6	37.5 ± 0.5	0.3582
Day 3	37.7 ± 0.5	37.5 ± 0.6	0.0852
Day 4	37.5 ± 0.6	37.4 ± 0.6	0.4398
Day 5	37.3 ± 0.4	37.4 ± 0.8	0.7006
Maximum	37.9 ± 0.5	37.9 ± 0.6	0.8893

Abbreviations: BT, body temperature; CRP, C-reactive protein; Day X, Xth hospital day; OI, oxygenation impairment; WBC, white blood cell.

cutoff score determined by the ROC curve was set as 2 or greater (sensitivity: 89.7%, specificity: 62.5%, positive predictive value: 70.0%, and negative predictive value: 86.2%).

Discussion

Oxygenation Impairment in Type-B AAD

The incidence of OI in patients with distal AAD (type-B AAD) has been reported to be 39 to 51%,[7,8,10] and the same results were obtained in our study (39 of 79 type-B AAD, 49.4%). Pathological studies have shown that inflammatory changes in the aortic wall occur during the course of AAD.[18,19] In addition, Piantadosi and Schwartz reported that activated neutrophils release toxic mediators that destroy the pulmonary capillary endothelium and increase vascular permeability, thereby leading to alveolar fluid accumulation that causes respiratory failure.[20] Recently, Furusawa et al reported that inhibiting the activity of neutrophil elastase may attenuate

Table 3 Factors (on admission day) associated with oxygenation impairment

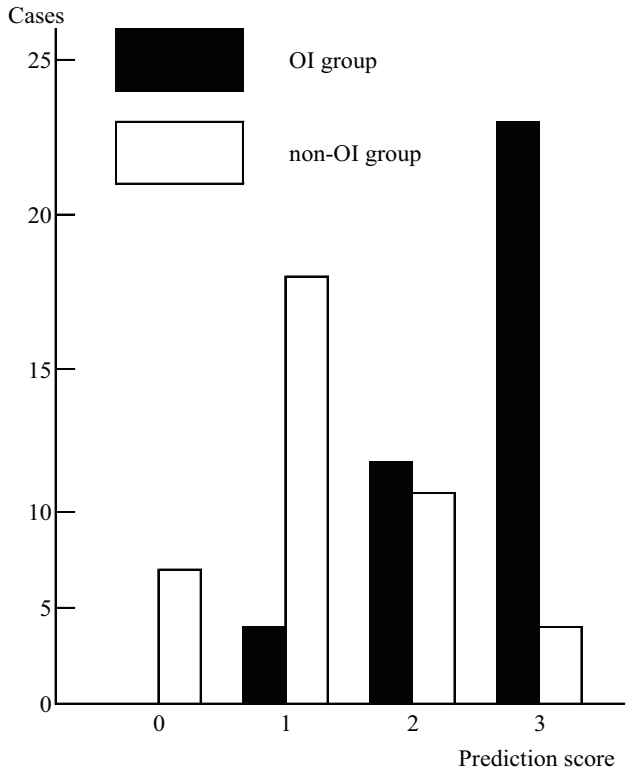
	Total	OI group	Non-OI group	*p* value
	n = 79	*n* = 39	*n* = 40	
Age < 68 years	37 (46.8)	25 (64.1)	12 (30.0)	0.0024
Male gender	52 (65.8)	30 (76.9)	22 (55.0)	0.0400
Body mass index ≥ 22 kg/m^2	57 (72.2)	36 (92.3)	21 (52.5)	< 0.0001
Maximum BT on admission day > 36.5°C	47 (59.5)	29 (74.4)	18 (45.0)	0.0079
DeBakey IIIb	66 (83.5)	36 (92.3)	30 (75.0)	0.0381
Patent or partial thrombosed false lumen	32 (40.5)	21 (53.8)	11 (27.5)	0.0171
P_{O_2}/F_{IO_2} on admission < 300	41 (51.9)	31 (79.5)	10 (25.0)	< 0.0001

Abbreviations: BT, body temperature; OI, oxygenation impairment.
Note: Number of cases in percentages.

Table 4 Multivariate analysis of factors associated with oxygenation impairment

	p value	Odd ratio	95% confidence interval
Age < 68 years	0.1255	2.9447	0.7396–11.7241
Male gender	0.6692	0.7321	0.1751–3.0605
Body mass index ≥ 22 kg/m^2	0.0194	7.4885	1.3841–40.5148
Maximum BT on admission day > 36.5°C	0.0123	5.7438	1.4621–22.5648
DeBakey IIIb	0.2295	3.0863	0.4911–19.3946
Patent or partial thrombosed false lumen	0.0847	3.4216	0.8451–13.8529
Po_2/Fio_2 on admission < 300	0.0161	5.2222	1.3594–20.0613

Abbreviation: BT, body temperature.



	OI group	non-OI group
Prediction score≥ 2	35	15
Prediction score≤ 1	4	25

sensitivity	89.7%	(35/39)
specificity	62.5%	(25/40)
positive predictive value	70.0%	(35/50)
negative predictive value	86.2%	(25/29)

Fig. 2 Predicting the occurrence of OI in patients with type-B acute aortic dissection. The applicable number of three factors associated with OI (body mass index ≥ 22 kg/m^2, maximum body temperature on the admission day > 36.5°C, and Po_2/Fio_2 ratio on admission < 300) was defined as the prediction score. This score was able to predict the occurrence of OI when the cutoff value was set at point 2 or greater. OI, oxygenation impairment.

postoperative respiratory complications in patients with AAD.[21] In addition, it has been reported that pleural effusion frequently occurs in patients with AAD, often in association with inflammatory reactions, including high body temperatures and increased WBC counts and serum CRP levels.[22] The occurrence of OI has been reported to be strongly associated with active inflammatory reactions, including high WBC counts, serum CRP levels, and body temperatures.[7,8,10] These active inflammatory reactions were also demonstrated in the present study.

Kurabayashi et al found that respiratory failure in AAD patients appears to be closely correlated with the degree of aortic injury measured on precise evaluation of CT films, possibly mediated by the magnitude of the systemic inflammatory reaction to the aortic injury.[10] Our results also showed that OI occurred more frequently in the patients with larger aortic dissections (DeBakey IIIb) than those with DeBakey IIIa aortic dissections.

During this decade, sleep apnea syndrome has been reported to be a risk factor for the development of cardiovascular diseases, including AAD.[23–29] In addition, sleep apnea is frequently observed in obese patients.[30–34] Therefore, we suggest that high body mass indices may be associated with the occurrence of OI based on the results of this study. However, the relationship between sleep apnea and OI was not investigated in this retrospective study.

Clinical Factors Affecting Oxygenation Impairment

In this study, the peak levels of serum CRP and WBC count were associated with the occurrence of OI in type-B AAD patients. These findings have been reported previously, and higher levels of serum CRP after distal type AAD are associated with a higher incidence of OI and poor clinical outcomes in patients with aortic and peripheral artery diseases.[7,8,11–13] Systemic activation of the inflammatory system after aortic injury may play an important role in the development of OI. Although previous reports have found that the peak values of WBC counts, serum CRP levels, and body temperature are associated with OI, these values are inappropriate for predicting the occurrence of OI because they were measured after the occurrence of OI.

Except for the presence of inflammatory reactions, factors regarding patient backgrounds, including younger age, male gender, and nonslender frame, were associated with the

occurrence of OI in this study. We were unable to evaluate sleep apnea, though there may be a relationship between obesity, sleep apnea, and OI in AAD patients.

Predicting the Occurrence of Oxygenation Impairment

Although factors affecting OI such as WBC count, CRP levels, and body temperature have been previously reported,[7,8,11–13] the possibility of predicting the occurrence of OI has not yet been investigated. Therefore, we evaluated this relationship using factors measured before the occurrence of OI in type-B AAD patients. In the present study, OI occurred on hospital day 2.5 in the AAD patients, and we investigated factors measured on the admission day. In this study, we adopted the following factors for predicting the occurrence of OI: age, gender, body mass index, maximum body temperature on the admission day, type of AAD (the presence of a patent false lumen and DeBakey IIIa or IIIb), and P/F ratio on admission. The serum levels of CRP and WBC count were not used because increases in these levels were observed after the occurrence of OI. In addition, the multivariate analysis revealed that nonslender frame, relatively high maximum body temperature on the admission day, and lower P/F ratio on admission were more strongly associated with the occurrence of OI than the other factors.

To predict the occurrence of OI in type-B AAD patients, predictive scores were calculated according to the number of the following three applicable factors: nonslender frame (BMI $\geq$ 22 kg/m^2), relatively high maximum body temperature on the admission day ($>$ 36.5°C), and a lower P/F ratio on the admission day ($<$ 300). When the cutoff values were set at point 2 or greater, the scores were able to predict the occurrence of OI in type-B AAD patients with a high predictive value. We state here that this scoring system for predicting the occurrence of OI could be made available in the clinical setting of almost every institute.

Study Limitations

First, this study was conducted at only one university hospital, and the number of cases was small. Second, there was a lack of precise data regarding coagulation findings including D-dimer due to the retrospective design. Last, we were not able to evaluate the presence of sleep apnea in individual cases. Therefore, conducting a large cohort study is recommended to address these problems.

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