Admission white blood cell count predicts short-term clinical outcomes in patients with uncomplicated Stanford type B acute aortic dissection

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Abstract

Objectives Inflammation has been shown to be related with acute aortic dissection (AAD). The present study aimed to evaluate the association of white blood cell counts (WBCc) on admission with both in-hospital and long-term all-cause mortality in patients with uncomplicated Stanford type B AAD.

Methods From 2008 to 2010, a total of 377 consecutive patients with uncomplicated type B AAD were enrolled and then followed up. Clinical data and WBCc on admission were collected. The primary end points were in-hospital death and long-term all-cause death. Results The in-hospital death rate was 4.2%, and the long-term all-cause mortality rate was 6.9% during a median follow-up of 18.9 months. WBCc on admission was identified as a risk factor for in-hospital death by univariate Cox regression analysis as both a continuous variable and a categorical variable using a cut off of 11.0 × 10^9 cell/L (all \( P < 0.05 \)). After adjusting for age, sex and other risk factors, elevated admission WBCc was still a significant predictor for in-hospital death as both a continuous variable (hazard ratio [HR]: 1.052, 95% CI: 1.024–1.336, \( P = 0.002 \)) and a categorical variable using a cut off of 11.0 × 10^9 cell/L (HR: 2.056, 95% CI: 1.673–5.253, \( P = 0.034 \)). No relationship was observed between WBCc on admission and long-term all-cause death.

Conclusions Our results indicate that elevated WBCc upon admission might be used as a predictor for increased risk of in-hospital death in uncomplicated type B AAD. There might be no predictive value of WBCc for the long-term survival of type B AAD.

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Keywords: Acute aortic dissection; In-hospital mortality; Stanford type B; Survival; White blood cell

1 Introduction

Stanford type B acute aortic dissection (AAD) has a relatively high mortality rate even though diagnostic and therapeutic techniques have made great progress. Patients with type B AAD do not require open surgical treatment unless complicated by recurrent or refractory pain, organic malperfusion, acute renal failure, refractory hypotension, shock, progression aneurysmal dilatation or aortic rupture.[1-3] A previous study showed that the early prognosis in patients with type B AAD is relatively better than that in patients with Stanford type A AAD.[3] Uncomplicated type B AAD refers to stable patients without these complications and with a higher in-hospital survival rate (approximately 90%); however, reports from the International Registry of Aortic Dissection (IRAD) indicated that the long-term survival was not very satisfactory, even in those “lower risk” patients after hospital discharge.[4] Thus, predictive factors for clinical outcomes of type B AAD still need to be determined and might be useful.

Inflammation underlies both the pathogenesis and prognosis in patients with AAD.[5-8] High levels of biomarkers associated with generalized inflammation [C-reactive protein (CRP),[9-11] D-dimer,[10-17] platelet,[18,19] and fibrinogen[20] have been shown to indicate increased mortality re-
lared to AAD. Additionally, the recall and activation of macrophages inside the middle layer of the aorta were observed in the early phases of AAD, which indicated that white blood cells may play a crucial role in the progression of inflammation in AAD. White blood cell count (WBCc) is a sensitive and nonspecific marker of the acute inflammatory response, and our previous study confirmed that elevated WBCc upon admission increased the risk of in-hospital death in patients with type A AAD. However, the data regarding the association of WBCc upon admission and follow-up outcome were poorly defined in patients with type B AAD. Thus, the purpose of this study was to examine and analyse the prognostic effect of WBCc on short- and long-term outcomes in patients with uncomplicated type B AAD.

2 Methods

2.1 Patients

From October 2008 to December 2010, consecutive patients with suspected type B AAD who were admitted to the emergency centre of Fuwai Hospital were enrolled in this study. The diagnosis of type B AAD was confirmed by multi-detector computed tomography scanning. Stanford type B (DeBakey III) dissection was defined as a dissection not involving the ascending aorta and/or aortic arch, according to previously published criteria. Uncomplicated Stanford type B AAD was defined as stable patients without any of the following symptoms or signs at presentation and during the hospital course: recurrent or refractory pain, organic malperfusion, acute renal failure, refractory hypertension, hypotension/shock, progression aneurysmal dilatation or aortic rupture. Patients were excluded if they had a clear aetiology, such as Marfan syndrome, Loey-Dietz syndrome, iatrogenic aortic dissection (AD) secondary to cardiac surgery, thoracic endovascular aortic repair, a history of surgery for AD, or chronic AD. The in-hospital survival analysis included all patients in this study, and the long-term survival analysis included only discharged patients. This study was approved by the ethical committees of Fuwai Hospital, and written informed consent was obtained from each patient.

2.2 Data collection and clinical outcomes

Baseline characteristic data were recorded. Blood samples were obtained within 5 min after admission to the hospital, and the total WBCc was measured in the whole-blood specimen. To address the confounding effect of other inflammatory factors, CRP, D-dimer, and platelet count were assessed simultaneously. Other recorded clinical characteristics included baseline vital signs upon admission, imaging examinations and hospital management. The rationale and strategy of the surgical techniques were determined by experienced surgeons in the Department of Cardiovascular Surgery in our hospital. All patients were followed during hospitalization and subsequently via outpatient clinical visits or interim telephone calls until the occurrence of death or loss to follow-up. In-hospital mortality was defined as death within 30 days after admission to the emergency department. Long-term mortality was defined as an all-cause death after 30 days during the follow-up period.

2.3 Statistical analysis

All of the statistical analyses were performed using SPSS version 19.0 (SPSS, Inc., Chicago, Illinois, USA). Continuous variables are presented as mean ± SD or medians and interquartile ranges (IQRs) according to whether the variables conformed to a normal distribution and were compared using Student’s t test or the Mann Whitney rank-sum test. Categorical data are presented as numbers and percentages and were compared using the χ² or Fisher’s exact test. The analysis was stratified according to WBCc (> 11.0 × 10⁹ cells/L or ≤ 11.0 × 10⁹ cells/L as the cut off value for normal) according to previous studies. In-hospital and long-term clinical outcomes were determined using the Kaplan-Meier method and compared using the log rank test. A Cox proportional hazards regression model was used to assess the predictive role of WBCc in short- and long-term mortality with hazard ratios (HRs) and 95% confidence intervals (CIs). Two separate multivariate Cox models were constructed with the WBCc values entered as continuous data, using a cut off value of 11.0 × 10⁹ cells/L. Other variables selected for testing in the multivariate analysis were variables with a P value < 0.05 in the univariate models or variables that were thought to have an impact on AAD prognosis. Subgroup analyses were also performed using the Kaplan-Meier method, and the results were compared using the log-rank test. A P value < 0.05 was considered statistically significant.

3 Results

3.1 Participants and descriptive data

From 2008 to 2010, 492 consecutive individuals were diagnosed with type B AAD in Fuwai Hospital. After excluding 115 subjects who met the exclusion criteria, a total of 377 patients were enrolled in this study (detailed flow
The average follow-up period was 18.9 months (IQR: 10.9–37.0 months). All patients had a baseline WBCc available, and the follow-up rates were 100% at 30 days and 80.6% at 1 year. The follow-up time for 70 subjects was less than one year, and no event occurred during this period. Three subjects were eliminated from the study process due to loss of follow-up after discharge.

The mean age of all patients was 52.4 ± 11.8 years, and 85.7% of patients (323/377) were male. The baseline clinical characteristics of all patients stratified by WBCc (> 11.0 × 10^9 cells/L or ≤ 11.0 × 10^9 cells/L) are shown in Table 1. Patients with an elevated WBCc were younger and had a higher heart rate. Additionally, these patients had elevated CRP levels and ascending aorta diameters but had lower platelet counts (all P < 0.05). The average hospitalization period was 11 days (IQR: 8–16 days).

### 3.2 In-hospital and long-term outcome data

The overall in-hospital mortality rate was 4.2% (16/377), and a total of 361 patients were discharged from the hospital. During the follow-up, the long-term all-cause mortality rate was 6.9% (25/361). As shown in Figure 2A, a Kaplan-Meier analysis showed that the cumulative in-hospital survival rate was significantly lower in patients with an elevated admission WBCc (> 11.0 × 10^9 cells/L) compared to those with a normal WBCc (≤ 11.0 × 10^9 cells/L).

**Figure 1. Participant flow chart.** AAD: acute aortic dissection; IQR: interquartile ranges; WBCc: white blood cell count.

### Table 1. Baseline characteristics according to admission white blood cell count.

|                         | WBCc > 11.0 × 10^9/L (n = 127) | WBCc ≤ 11.0 × 10^9/L (n = 250) | P value |
|-------------------------|---------------------------------|---------------------------------|---------|
| Age, yrs                | 50.2 ± 9.9                      | 53.6 ± 12.6                     | 0.009   |
| Male                    | 109 (85.8%)                     | 214 (85.6%)                     | 1.000   |
| Hypertension            | 98 (77.2%)                      | 191 (76.4%)                     | 0.898   |
| Diabetes mellitus       | 5 (3.9%)                        | 17 (6.8%)                       | 0.354   |
| Coronary artery disease | 3 (2.4%)                        | 17 (6.8%)                       | 0.088   |
| Smoking history         | 70 (55.1%)                      | 121 (48.4%)                     | 0.232   |
| Alcohol history         | 32 (25.2%)                      | 77 (30.8%)                      | 0.281   |
| Duration of pain, h     | 15.0 (6.0–24.0)                 | 17.0 (5.0–30.0)                 | 0.053   |
| SBP, mmHg               | 136.7 ± 39.2                    | 147.9 ± 30.3                    | 0.458   |
| DBP, mmHg               | 74.7 ± 21.2                     | 85.8 ± 19.9                     | 0.244   |
| Heart rate, beats/min   | 80.0 (72.0–93.0)                | 78.0 (69.0–85.0)                | < 0.001 |
| White blood cell count, ×10^9/L | 13.5 (12.1–15.9) | 8.1 (6.5–9.5)                  | < 0.001 |
| Platelet count, ×10^9/L | 174.0 (151.0–217.0)             | 195.0 (153.0–259.0)             | 0.040   |
| C reaction protein, mg/L | 65.9 (23.2–102.0)              | 20.0 (6.6–64.4)                 | < 0.001 |
| D-dimer, μg/ml          | 2.5 (0.9–6.2)                   | 1.5 (0.5–4.3)                   | 0.371   |
| Creatinine, μmol/L      | 88.9 (72.8–107.9)               | 86.0 (74.2–103.1)               | 0.274   |
| Ascending aorta diameter, mm | 36.1 ± 5.2                     | 34.9 ± 5.2                      | 0.045   |
| Pericardial effusion    | 7 (5.5%)                        | 22 (8.8%)                       | 0.310   |
| Treatments              |                                 |                                 |         |
| β-blocker               | 119 (93.7%)                     | 232 (92.8%)                     | 0.832   |
| CCB                     | 106 (83.5%)                     | 218 (87.2%)                     | 0.349   |
| ACEI                    | 58 (45.7%)                      | 117 (46.8%)                     | 0.913   |
| ARB                     | 46 (36.2%)                      | 70 (28.0%)                      | 0.125   |
| TEVAR                   | 135 (54.0%)                     | 57 (44.9%)                      | 0.094   |

Data are presented as mean ± SD, n (%), or medians (interquartile ranges). ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptors blockers; CCB: calcium channel blocker; DBP: diastolic blood pressure; SBP: systolic blood pressure; TEVAR: thoracic endovascular aneurysm repair; WBCc: white blood cell count.
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Figure 2. Kaplan-Meier curve for in-hospital and long-term survival stratified by admission WBCc cut off value (11.0 × 10^9 cells/L). (A): In the in-hospital (30 day) survival rate was lower in patients with elevated WBCc (> 11.0 × 10^9 cells/L, log-rank \( P = 0.012 \)); (B): the long-term survival rate was comparable in patients after discharge stratified by admission WBCc cut off value (11.0 × 10^9 cells/L, log-rank \( P > 0.05 \)). WBCc: white blood cell count.

3.3 Effect of elevated admission WBCc on in-hospital death in uncomplicated type B AAD

The results of the univariate Cox regression analysis of predictors of in-hospital mortality are shown in Table 2. WBCc upon admission was associated with in-hospital mortality as both a continuous variable (HR = 1.059, 95% CI: 1.018–1.102, \( P = 0.004 \)) and a categorical variable with a cut off value of > 11.0 × 10^9 cells/L (HR = 3.396, 95% CI: 1.234–9.344, \( P = 0.018 \)). Other factors associated with 30-day mortality included admission heart rate, CRP level, serum creatinine level and thoracic endovascular aortic repair (TEVAR). Multivariate-adjusted HRs for 30-day mortality according to 1.0 × 10^9 cells/L increase and according to the cut off value of 11.0 × 10^9 cells/L are presented in Table 3. After adjusting for age, sex, and other risk factors (TEVAR was not included because of its great interference in modelling), elevated admission WBCc was still an independent predictor for in-hospital mortality when considered as a continuous variable and a categorical variable (HR = 1.052, 95% CI: 1.024–1.336, \( P = 0.002 \)) using a cut off value of 11.0 × 10^9 cells/L (HR = 2.056, 95% CI: 1.673–5.253, \( P = 0.034 \)). Serum creatinine (continuous) was also an independent risk factor for in-hospital mortality in two Cox models.

3.4 Effect of elevated admission WBCc on long-term mortality in uncomplicated type B AAD

In discharged patients (n = 361), a univariate Cox analysis did not reveal an association between WBCc and long-term mortality (Table 4). A multivariate Cox regression analysis also showed no association between long-term mortality and admission WBCc (Table 5). The two Cox models revealed that age and the serum creatinine level were independent risk factors for long-term mortality, and TEVAR was the main protective factor associated with long-term survival.

3.5 Subgroup analyses of short- and long-term outcomes in uncomplicated type B AAD

For further analysis, patients stratified by admission WBCc were divided into different subgroups (age, gender, comorbidity and intervention). As shown in Table 6, the risk of in-hospital mortality was significantly higher in patients with an elevated WBCc who were male, were older than 60 years of age, and only received conservative treatment (all log-rank \( P < 0.05 \)). Although the Kaplan-Meier analysis could not be performed for the subgroup that received TEVAR treatment, no short-term events were observed to be related to WBCc upon admission. No differences were
observed in the long-term survival rate between all the subgroups.

4 Discussion

This observational retrospective study based on a large sample cohort analysed the association of admission WBCc in uncomplicated type B AAD patients with short- and long-term clinical outcomes. Our results showed that patients with elevated admission WBCc were younger, had higher admission heart rate and had larger ascending aorta diameters. Additionally, these patients had elevated CRP.

Table 2. Predictors of 30-day mortality by univariate Cox analysis.

| Variables                      | HRs  | 95%CI  | P value |
|--------------------------------|------|--------|---------|
| Age, per year (continuous)     | 0.967| 0.927–1.009 | 0.124  |
| Sex (male vs. female)          | 2.788| 0.969–8.025 | 0.057  |
| Hypertension                   | 0.662| 0.230–1.905 | 0.444  |
| Coronary artery disease        | 1.182| 0.156–8.949 | 0.871  |
| Duration of pain, per hour (continuous) | 0.995| 0.980–1.012 | 0.580  |
| SBP (continuous)               | 0.987| 0.878–1.110 | 0.833  |
| Heart rate (continuous)        | 1.043| 1.013–1.075 | 0.005  |
| WBCc, per 1×10^9 cells/L (continuous) | 1.059| 1.018–1.102 | 0.004  |
| WBCc ≤ 11.0 ×10^9/L            | Reference | - - |         |
| WBCc > 11.0 ×10^9/L            | 3.396| 1.234–9.344 | 0.018  |
| Platelet count, per 1×10^9 cells/L (continuous) | 1.005| 0.999–1.010 | 0.081  |
| C reaction protein, per 1 mg/L (continuous) | 1.008| 1.002–1.014 | 0.008  |
| D-dimer, per 1 mg/L (continuous) | 1.050| 0.929–1.188 | 0.434  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.006| 1.002–1.010 | 0.004  |
| AAD, per 1 mm (continuous)     | 0.993| 0.897–1.100 | 0.898  |
| Pericardial effusion           | 0.789| 0.104–5.975 | 0.819  |
| TEVAR                          | 0.380| 0.001–0.792 | 0.038  |

AAD: ascending aorta diameter; SBP: systolic blood pressure; TEVAR: thoracic endovascular aneurysm repair; WBCc: white blood cell count.

Table 3. Independent predictors of in-hospital mortality by multivariable Cox analysis.

| Variables                      | HRs  | 95% CI | P value |
|--------------------------------|------|--------|---------|
| Model 1                        |      |        |         |
| WBCc, per 1×10^9/L (continuous) | 1.052| 1.024–1.336 | 0.002  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.006| 1.002–1.032 | 0.005  |
| Model 2                        |      |        |         |
| WBCc ≤ 11.0 ×10^9/L            | Reference | - - |         |
| WBCc > 11.0 ×10^9/L            | 2.056| 1.673–5.253 | 0.034  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.004| 1.001–1.027 | 0.015  |

Variables included in the multivariate Cox models were age (continuous), sex, C-reactive protein (continuous), platelet count (continuous), D-dimer, and serum creatinine (continuous). WBCc: white blood cell count.

Observed in the long-term survival rate between all the subgroups.

Table 4. Predictors of long-term mortality by univariate Cox analysis.

| Variables                      | HRs  | 95% CI | P value |
|--------------------------------|------|--------|---------|
| Age, per year (continuous)     | 1.074| 1.036–1.112 | <0.001 |
| Sex (male vs. female)          | 1.194| 0.357–3.997 | 0.774  |
| Hypertension                   | 1.186| 0.445–3.160 | 0.733  |
| Coronary artery disease        | 1.462| 0.345–6.201 | 0.607  |
| Duration of pain, per hour (continuous) | 1.000| 0.995–1.004 | 0.880  |
| SBP (continuous)               | 0.975| 0.937–1.015 | 0.212  |
| Heart rate (continuous)        | 1.022| 0.995–1.049 | 0.108  |
| WBCc, per 1×10^9 cells/L (continuous) | 0.953| 0.851–1.067 | 0.406  |
| WBCc ≤ 11.0 ×10^9/L            | Reference | - - |         |
| WBCc > 11.0 ×10^9/L            | 0.828| 0.346–1.983 | 0.672  |
| Platelet count, per 1×10^9 cells/L (continuous) | 0.993| 0.986–0.999 | 0.031  |
| C reaction protein, per 1 mg/L (continuous) | 1.005| 0.996–1.014 | 0.253  |
| D-dimer, per 1 mg/L (continuous) | 1.047| 0.916–1.196 | 0.498  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.008| 1.003–1.012 | <0.001 |
| AAD, per 1 mm (continuous)     | 1.109| 0.997–1.235 | 0.057  |
| Pericardial effusion           | 1.340| 0.761–2.352 | 0.314  |
| TEVAR                          | 0.168| 0.058–0.490 | 0.001  |

Variables included in both the multivariate Cox models were age (continuous), sex, C-reactive protein (continuous), platelet count (continuous), D-dimer, and serum creatinine (continuous). The variable WBCc was included as a continuous variable in Model 1 and as a categorical variable using a cut off value of 11.0 × 10^9 cells/L in Model 2. TEVAR: thoracic endovascular aneurysm repair; WBCc: white blood cell count.

Table 5. Predictors of long-term mortality by multivariate Cox analysis.

| Variables                      | HRs  | 95% CI | P value |
|--------------------------------|------|--------|---------|
| Model 1                        |      |        |         |
| Age, per years (continuous)     | 1.048| 1.014–1.085 | 0.010  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.005| 1.001–1.009 | 0.008  |
| TEVAR                          | 0.241| 0.081–0.731 | 0.011  |
| Model 2                        |      |        |         |
| Age, per years (continuous)     | 1.054| 1.019–1.091 | 0.002  |
| Serum creatinine, per 1 μmol/L (continuous) | 1.006| 1.002–1.010 | 0.003  |
| TEVAR                          | 0.236| 0.079–0.705 | 0.010  |

Variables included in both the multivariate Cox models were age (continuous), sex, C-reactive protein (continuous), platelet count (continuous), D-dimer, and serum creatinine (continuous). The variable WBCc was included as a continuous variable in Model 1 and as a categorical variable using a cut off value of 11.0 × 10^9 cells/L in Model 2. TEVAR: thoracic endovascular aneurysm repair; WBCc: white blood cell count.

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Table 6. Subgroup Kaplan-Meier analyses for short- and long-term outcome stratified by WBCc.

| Variables | In-hospital outcome | Long-term outcome |
|-----------|---------------------|-------------------|
|           | WBCc > 11.0 × 10⁹/L | WBCc ≤ 11.0 × 10⁹/L | WBCc > 11.0 × 10⁹/L | WBCc ≤ 11.0 × 10⁹/L |
|           | (No. of events/No. of total) | (No. of events/No. of total) | (No. of events/No. of total) | (No. of events/No. of total) |
| Age       |                      |                   |                      |                   |
| > 60 years| 1/17 0/71           | 4.176 0.041       | 3/16 16/71          | 0.027 0.790       |
| ≤ 60 years| 9/110 6/179         | 3.329 0.068       | 4/101 7/173         | 0.067 0.796       |
| Gender    |                      |                   |                      |                   |
| Male      | 7/109 4/214         | 4.638 0.031       | 6/102 16/210        | 0.232 0.630       |
| Female    | 3/18 2/36           | 1.789 0.181       | 1/15 2/34           | 0.635 0.628       |
| Co-morbidity |                   |                   |                      |                   |
| Hypertension | 8/98 3/191      | 7.798 0.005       | 6/90 14/188         | 0.008 0.929       |
| Non-hypertension | 2/29 3/59       | 0.136 0.712       | 1/27 4/56           | 0.106 0.744       |
| Intervention |                   |                   |                      |                   |
| TEVAR     | 0/57 0/135         | * 2/57 2/135      | 0.863 0.353         |                   |
| Non-TEVAR | 10/70 6/115        | 4.729 0.030       | 5/60 16/109         | 0.949 0.330       |

* Kaplan-Meier analysis could not be performed because no events occurred. TEVAR: thoracic endovascular aneurysm repair; WBCc: white blood cell count.

levels but had lower platelet counts. A marked elevated WBCc upon admission in patients with type B AAD was associated with poor short-term outcomes. However, the long-term mortality rate did not differ between patients with elevated or normal WBCc upon admission. After adjustment using a multivariate Cox analysis, the effect of elevated admission WBCc on in-hospital mortality in patients with uncomplicated type B AAD was still significant, but it did not increase the risk of long-term mortality. Our study also confirmed that TEVAR was an independent protective factor that could significantly reduce long-term mortality. Moreover, a subgroup analysis showed that elevated WBCc upon admission carried an excess risk of in-hospital mortality only in patients who were medically managed (non-TEVAR), elderly (more than 60 years of age), male, and with hypertension.

Inflammatory pathways are involved in aortic rupture in both type A and type B Stanford AAD. Immune infiltrate has been observed within the middle and outer layers of dissected aortic specimens. It has also been observed that the recall and activation of macrophages inside the middle tunic are key events in the early phases of AAD. Macrophages release metalloproteinases and pro-inflammatory cytokines that contribute to matrix degradation and neoangiogenesis underlying aortic wall remodelling and wall weakness in dissections. The WBCc is a sensitive and non-specific inflammatory marker. In the present study, approximately one-third of the patients showed an elevated WBCc upon admission. Those patients also had a higher level of CRP, higher heart rate, and lower platelet counts, which indicated the presence of acute inflammatory responses.

Recent studies revealed that indicators of the inflammatory reaction (WBCc, PLTc, D-dimer level, and CRP level) are closely associated with clinical outcomes in aortic events. Studies showed that an elevated WBCc increased the risk of in-hospital death in Stanford type A AAD patients. A French study with a Western cohort (n = 94) revealed that the WBCc failed to predict in-hospital death (OR = 2.80, 95% CI: 0.80–12.58, P = 0.12) in AAD (both Stanford type A and type B). However, the sample size in that study was relatively small, and the patients with type B AAD were not specified. Our results showed a higher risk of in-hospital death in uncomplicated type B AAD patients whose admission WBCc was elevated above the normal range (> 11.0 × 10⁹ cell/L), which was consistent with our previous findings in type A AAD. However, WBCc failed to predict long-term outcomes in our study cohort. Leukocyte count increased in the acute phase of inflammation, and its level decreased quickly back to the normal range within 4 weeks after admission in the powerful treatment process in AAD. Perhaps this observation explains why we failed to find an association between admission WBCc and long-term survival in type B AAD.

Although the management of newly diagnosed type B AAD remains controversial, conservative therapy is still recommended. Traditional surgical treatments are recommended for patients who develop complications, such as progression of dissection, aortic rupture, organic malperfusion, aneurysmal dilatation and refractory pain. However, surgical resection of the thoracic aorta is still associated with high mortality and morbidity from complications despite remarkably improved operative techniques. Because of the continued success of TEVAR, this procedure has been extended to treat type B AAD in selected patients and
has been associated with encouraging outcomes.\textsuperscript{[30,31]} This technique provides an attractive and less invasive alternative therapy for type B AAD. According to ADSORB (Acute Dissection: Stent graft OR Best medical therapy) trial’s report, the all-cause mortality in a 1-year follow-up was reduced to 3.3\% in TEVAR-treated patients with uncomplicated type B aortic dissection.\textsuperscript{[32]} In our cohort, more than half (192/377) of the patients underwent endovascular repair, and no deaths occurred in the hospital. In the long-term survival analysis, our results showed that TEVAR was the only independent protective factor after adjustment. Therefore, our results confirm TEVAR’s promising protective role in improving the long-term survival in type B AAD, independent of the WBCc upon admission.

In the subgroup analysis, we also found that elevated admission WBCc carried an excess in-hospital mortality risk only in patients who were non-TEVAR patients, elderly, male and with hypertension. We identified increasing age as an independent risk factor in long-term mortality in our multivariable Cox regression analysis. A similar result was observed in the investigation of IRAD, in which complicated type B AAD in the elderly (> 70 years of age) was associated with a higher mortality risk.\textsuperscript{[33]} The authors explained that the great number of pre-existing comorbidities in the elderly patients and advanced age were risk factors for mortality after thoracic aortic intervention. The present results indicated that elderly patients with elevated WBCc upon admission were at a high risk of in-hospital death, and more severe measures may need to be performed in those individuals. The presentation of AAD varies with a patient’s sex, and the effects of gender on the outcomes of type B AAD currently remain controversial. Traditionally, aortic disease affects men more frequently than women. Current observational data indicate that the symptoms of AAD are less typical in female patients, thus causing delayed diagnosis and worse outcomes.\textsuperscript{[34]} However, in type B AAD, the effect of gender on clinical outcome has not been clarified. In this study, although the in-hospital mortality stratified by admission WBCc was significantly different in male but not female patients, we could not easily draw a conclusion with certainty because of the relatively small sample size of females (n = 54). From our previous and present studies,\textsuperscript{[33]} gender and hypertension were not independent predictors of early events in type B AAD. However, perhaps as the non-independent risk factors began to accumulate, the negative effect of the inflammatory reaction on early outcome will gradually emerge.

Several limitations need to be mentioned in the present study. First, this study is a single-centre observational study. Our results may not be representative of those from patients in other centres because the patient volume and experiences in the management of type B AAD may differ between our centre and other centres. However, the reliability of our results was strongly enhanced by our large sample size and the consideration of both short-term and long-term outcomes of AAD. Second, our study only analysed the WBCc measured within 5 min of admission. The analysis of a series of WBCc measurements at different time points may provide more valuable information for evaluating the prognostic role of WBCc in AAD. Thus, additional research is needed to understand the role of admission WBCc, either alone or in combination with other circulating inflammatory biomarkers, in the risk stratification of AAD.

In conclusion, the present study indicates that elevated WBCc upon admission might be used as a predictor for the increased risk of in-hospital mortality in uncomplicated type B AAD. However, there might be no predictive role of WBCc for the long-term survival of uncomplicated type B AAD.

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