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Original Article

Relationship between normal preoperative white blood cell count and major adverse events after endovascular repair for abdominal aortic aneurysm: results of a pilot study☆,☆☆

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ABSTRACT

Study objective: To examine the association between preoperative white blood cell (WBC) count within the reference range and major adverse events (MAEs) following endovascular repair of abdominal aortic aneurysms (AAA).
Design: Prospective observational study.
Setting: Vascular surgery clinic in a tertiary university hospital.
Patients: One hundred fifty-three consecutive patients.
Intervention: Endovascular repair of AAA.
Measurements: All patients had normal preoperative WBC count (3.5-10.3 K/μL). *Postoperative MAE* was defined as death, stroke, and myocardial infarction. The prognostic value of preoperative WBC was determined by receiver operating characteristic curves, whereas χ^2 test and Cochran-Armitage trend test were used to assess the association between MAE and different values of WBC.
Main results: A preoperative WBC cutoff value of 7.3 K/μL could predict MAE with 62% sensitivity and 62% specificity (area under the curve, 0.62). Patients with higher preoperative WBC experienced more events compared with patients with lower values ($P = .027$). A linear relationship was observed between an increasing preoperative WBC count within the reference range and the risk of postoperative events ($P = .004$). Logistic regression analysis showed that preoperative normal WBC count was an independent predictor of MAE and revealed that for every 1-K/μL increase, patients had a 32.8% increase in their relative odds of developing postoperative MAE ($P = .035$).
Conclusions: This pilot study demonstrates a linear correlation between an increasing preoperative WBC count within the reference range and an increased risk for postoperative MAEs following endovascular repair for AAA. Identification of high-risk patients at an early stage by using WBC count could prove useful in implementing measures to improve their clinical outcome.

1. Introduction

Inflammation has a central role in the pathophysiology of atherosclerosis, and therefore several inflammatory biomarkers have emerged as predictors of cardiovascular morbidity [1]. White blood cell (WBC) count constitutes a simple marker of inflammation that has been associated with prediction of future cardiovascular events in several different populations, including patients with acute coronary syndrome and critical limb ischemia [2-4].

There are only a few studies investigating the prognostic role of WBC in vascular surgical patients. Toor et al [5] by assessing patients after percutaneous transluminal angioplasty found that preprocedural neutrophil count was an independent predictor of outcome and could be used for global risk factor assessment. A recent retrospective study of nearly 800 patients undergoing endovascular procedures found a strong

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correlation between an increased preoperative WBC within the reference range and an increased risk of major adverse events (MAEs) and death following endovascular interventions [6]. This study however failed to depict any difference in WBC prediction value in relation to different procedures, although a trend toward complications and MAEs following carotid artery stenting and endovascular aneurysm repair (EVAR) was noted.

An association between a normal WBC count and outcome measures such as cardiovascular events has not been investigated previously in patients undergoing endovascular aortic interventions. Preoperative WBC count might act as predictive factor for identifying patients at increased risk of complications after endovascular aneurysm repair for abdominal aortic aneurysm (AAA). The aim of this prospective study was to examine the association between preoperative WBC count and MAEs following endovascular repair of AAA.

2. Methods

2.1. Study sample

In a prospective study approved by the institutional review committee, all subsequent patients with AAA undergoing EVAR between January 2011 and September 2013 were eligible for inclusion. During this time, endovascular repair was offered to all suitable patients according to the European Society for Vascular Surgery practice guidelines for the management of AAA [7]. Exclusion criteria were defined as follows:

- Preoperative WBC outside the reference range (3.5-10.5 × 103/μL) as determined by the University Hospital of Ioannina Laboratory
- Signs of gangrene
- Previous trauma or surgery 2 months prior to enrollment
- Patients with previous implantation of endoprosthesis
- History of any autoimmune disease or systemic inflammatory condition
- Any type of malignancy
- Use of anti-inflammatory drugs, chemotherapeutic agents or immunosuppressants, or anticoagulants

2.2. Procedure

All patients were treated by the same surgical and anesthesiology team in a fully equipped operating room with the patient under general anesthesia. Induction and maintenance of anesthesia were performed in a standardized manner in all patients. All patients received two 14- to 16-gauge peripheral venous lines, a radial arterial line, and a Volley catheter. Operative monitoring included electrocardiography, pulse oximetry, invasive arterial blood pressure, skin temperature, and end-tidal carbon dioxide. Anesthesia was induced with propofol 1-2.5 mg/kg and fentanyl 1 μg/kg and maintained with sevoflurane in combination with air and oxygen. Endotracheal intubation was facilitated with 0.6 mg/kg rocuronium. The depth of anesthesia was measured by the bispectral index monitor, and values were maintained at 40-60. Additional rescue bolus doses of fentanyl 0.5-0.75 μg/kg were administered aiming to keep the heart rate and blood pressure within 20% of the baseline value. All patients received paracetamol 1 g intravenously and ondansetron 4 mg in the end of the procedure.

Every effort was made to follow the selection criteria recommended by the manufacturer of the stent graft. However, the surgeon's decision as to which device to use was based on anatomical characteristics of the proximal neck, the iliac artery configuration, and the presence of thrombus or calcification.

2.3. Variables of interest

Demographics, risk factors, preoperative medication, and perioperative complications were recorded for each patient. Adverse events included acute myocardial infarction (MI), ischemic stroke, and death of any cause.

2.4. Definition of cardiovascular events

The primary end point was a composite of death from cardiac causes, nonfatal acute MI, and ischemic stroke. Death was considered due to cardiac causes if the patient died of MI, cardiac arrhythmia, or congestive heart failure caused primarily by a cardiac condition. The diagnosis of MI required elevated troponin concentration with at least one of two 12-lead ECG changes, including development of new Q waves or new persistent ST-T segment or T-wave changes. *Stroke* was defined according to the World Health Organization definition as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting >24 hours or leading to death, with no apparent cause other than that of a vascular origin [8]. Transient ischemic attack included brief episodes of neurologic dysfunction resulting from focal cerebral ischemia, not associated with a permanent cerebral infarction, lasting <24 hours [9]. The diagnosis of ischemic stroke was made if signs or symptoms of ischemic stroke were confirmed with imaging studies.

2.5. Medication

All patients were under antiplatelet therapy (aspirin 100 mg once daily) for at least 3 weeks prior to the procedure. Preoperative medications were continued immediately after surgery. Patients who were enrolled and were already receiving statin continued their medication. For patients not already on statin, atorvastatin (20 mg once daily) was initiated at the screening visit.

2.6. Follow-up

All patients underwent a postoperative surveillance protocol at 1, 6, and 12 months, which included physical examination and computed tomographic angiography.

2.7. Blood samples

Venous blood was collected without tourniquet preoperatively. For the determination of WBC, 2 mL of blood was transferred into an evacuate tube containing 3.6 mg K ethylenediaminetetraacetic acid dry salt (Becton-Dickinson Vacutainer, Plymouth, UK). The blood was mixed with the anticoagulant by repeated inversions of the tube. Complete blood cell counts were measured in the SE-9500 model of Automated Hematology Analyzer (Sysmex Corp, Kobe, Japan).

2.8. Statistical analysis

This was a pilot study to evaluate the feasibility and inform the design of a larger observational study. No formal sample size calculation was made. Instead, we planned to recruit 150 patients undergoing EVAR. Data were expressed as mean ± standard deviation as appropriate or except for non-Gaussian parameters that are presented as median (range). Comparisons of continuous variables were performed by Student *t* test for normally distributed variables and Mann-Whitney *U* test for nonnormally distributed variables, whereas the χ^2 test was used for categorical variables. Preoperative WBC was compared in relation to each postoperative outcome by Student *t* test, and the risk ratios for postoperative complications across increasing subgroups of WBC were determined using univariate logistic regression. The Cochran-Armitage trend test was conducted to examine the linear trend between the WBC and postoperative outcomes. When a linear trend was