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SHORT COMMUNICATION

Number of erythrocytes as a prognostic marker in patients undergoing heart valve surgery

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INTRODUCTION

Anaemia is defined by the Word Health Organisation as a haemoglobin level < 130 g/L for men and < 120 g/L for women [1]. It has been shown that lower haemoglobin levels are associated with increased mortality and morbidity among the elderly, and in patients with chronic heart failure or myocardial infarction [2–4]. The role of haemoglobin or haematocrit as independent predictors of mortality and morbidity in patients undergoing cardiac surgery has been described primarily in patients with coronary artery disease undergoing coronary artery bypass grafting [5, 6], as well as in patients undergoing heart valve surgery or congenital heart defects surgery [7–9]. In contrast, the predictive role of the red blood cell count (RBC) in patients undergoing valvular cardiac surgery has not been described. Given this gap in knowledge, we decided to assess a predictive value of the individual parameters of blood cell counts in patients undergoing heart valve surgery.

METHODS

The current prospective study was performed on 500 consecutive patients with haemodynamically significant valve defects with no significant atherosclerotic lesions in carotid arteries and porcelain aorta, who underwent elective replacement or repair of the valve at the Institute of Cardiology, Warsaw, Poland between 2014 and 2016. Patients under 18 years of age, unwilling to participate, or diagnosed with active malignancy, autoimmune diseases, and chronic inflammatory bowel disease were excluded from the study. Once a consent for participation was obtained, the following data were collected: sex, age, body mass index, comorbidities, echocardiography findings, and the assessment of the coronary arteries. The new European System for Cardiac Operative Risk Evaluation (EuroSCORE II) calculator was used to estimate the risk of surgery for each patient. One day before surgery a blood sample for biomarker analysis was collected from each patient. Full blood counts were measured from K_2EDTA samples using a Sysmex K-4500 (Sysmex, Japan) electronic counter. Each patient was followed up for at least 30 days. A total of 498 procedures were performed via a midline sternotomy, one procedure via ministernotomy, and one procedure via a lateral thoracotomy incision, under general anaesthesia in normothermia (498 procedures) or mild hypothermia (two procedures). The primary endpoint was death from all causes. The follow-up of discharged patients was conducted through direct observation during hospitalisation, telephone interviews, and/or at outpatient clinic visits 30 days after the cardiac operation. The protocol was approved by the Institutional Ethics Committee.

Statistical analysis

Statistical analysis was performed using SAS version 9.2. Data are presented as the mean ± standard deviation (SD) and the frequency (%). Intergroup comparisons were made using the Mann-Whitney U test, the Pearson's χ^2 test, or Student t-test. Logistic regression was used to assess relationships between variables. The following covariates were investigated for their association with the endpoint in univariate analysis: age, body mass index, chronic kidney disease, EuroSCORE II, arterial hypertension, insulin-dependent diabetes mellitus, left ventricular ejection fraction, New York Heart Association class, preoperative atrial fibrillation, chronic obstructive airways disease, coronary artery disease, smoking status, dyslipidaemia, peripheral atherosclerosis, previous myocardial infarction, pulmonary blood pressure, stroke history, tricuspid annulus plane systolic excursion, creatinine, high sensitivity-C-reactive protein, high-sensitivity troponin T, haematocrit, haemoglobin, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, mean corpuscular volume, N-terminal-pro B-type natriuretic peptide, platelet count, RBC, red cell distribution width (RDW), and white blood cell count. Significant determinants ($p < 0.05$) identified from univariate analysis were subsequently entered into multivariate models. The predictive value of RBC was assessed by a comparison of the areas under the respective receiver operating characteristic

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curve (ROC). For the analysis of endpoint in the all-patient group, Kaplan-Meyer curves were used.

RESULTS

The study group included 500 consecutive patients who underwent replacement or repair of valve(s). The mean age was 62.6 ± 12.46 years, and 290 (58%) patients of the study population were men. The mean RBC level was 4.5 ± 0.5 10^{12}/L. The primary endpoint (death from all causes) occurred in 16 patients. Thirteen patients died as a result of gradually increasing multi-organ failure, one patient died because of early infective endocarditis, one patient died due to post-operative bleeding, and one patient died suddenly (the cause of death was not unequivocally established because an autopsy was not performed). In multivariate analysis, RBC (odds ratio [OR] 0.088; 95% confidence interval [CI] 0.022–0.341; p = 0.0005), RDW (OR 1.697; 95% CI 1.056––2.728; p = 0.02), and creatinine level (OR 1.013; 95% CI 1.001–1.026; p = 0.04) remained independent predictors of death. The optimal cut-off point for death was 3.67 10^{12}/L. The combined model EuroSCORE II calculation + RBC predicted 30-day mortality better (area under the receiver operating characteristic curve [AUROC] 0.827; 95% CI 0.728–0.926) than EuroSCORE II calculation alone (AUROC 0.808; 95% CI 0.713–0.903; p = 0.044; Fig. 1).

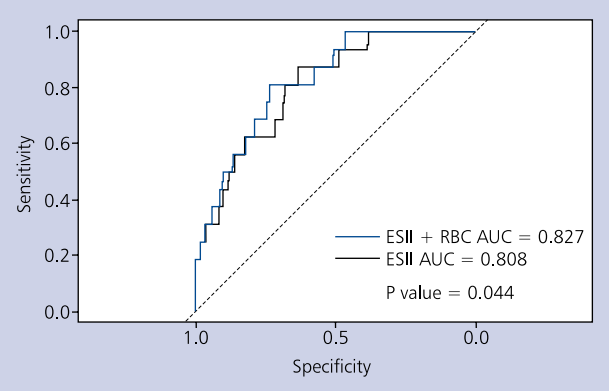

Figure 1. Areas under receiver operating characteristic (ROC) curves of EuroSCORE II (ESII) and ESII + red blood cell count (RBC) for a 30-day survival following valve replacement/repair surgery; AUC — area under the curve

DISCUSSION

Heart valve surgery is associated with the risk of serious postoperative complications, including death, prolonged hospitalisation, and increased cost of treatment, which does not always ensure therapeutic success. Numerous publications [10–13] have confirmed that the commonly used risk evaluation tools, EuroSCORE II, EuroSCORE, and Society of Thoracic Surgeons (STS), have limitations resulting from insufficient calibration models. To our knowledge, this is the first report showing the prognostic significance of RBC in predicting mortality in patients undergoing heart valve surgery at the 30-day follow-up. In the present study, the RBC parameter was found to be an independent predictor of death in 500 patients without significant atherosclerotic changes in the carotid arteries and porcelain aorta, although a significant predictive value in univariate analyses has also been established for other parameters of the red blood cell system, such as haematocrit and haemoglobin. Furthermore, the RBC parameter was the only one to significantly increase the predictive ability of the EuroSCORE II calculator.

RBC is a routinely evaluated parameter. Reduction of RBC may lead to a decrease in the amount of oxygen transported to each cell of the human body, and thus induce a deficit of oxygen in tissues, and anaerobic metabolism, which can have negative consequences, in particular in the perioperative period [4]. Available literature has demonstrated a significant correlation between increased levels of lactate as a marker of tissue hypoxia, higher incidence of heart failure, increased length of hospital stay, and higher postoperative mortality [14]. In the present group of patients, the most common cause of death was multiple organ failure, which may confirm the hypothesis of tissue hypoxia. Therefore, information about the prognostic value of the reduced RBC can provide additional information about the risk of cardiac valve surgery.

This was a single-centre study that included a diverse group of 500 participating patients. Only preoperative factors were evaluated in the study. Further studies are needed to explain the causes of the reduced value of RBC in patients with valvular heart disease and the pathomechanisms linking an increased risk of death in patients with a lower RBC.

In conclusion, the results of this study indicate that RBC is a useful parameter for estimating the risk in patients undergoing heart valve surgery. Moreover, the predictive ability of RBC, assessed by the area under the ROC curve, enhances the predictive ability of the EuroSCORE II calculator. Further investigation is required, and information about the prognostic value of RBC may provide an additional clue for physicians in identifying patients who will not benefit from surgical treatment or may be eligible for other therapeutic options.

Conflict of interest: *none declared*

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