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Original Article

Prognostic Impacts of Increases in Amino Transaminases Following Coronary Artery Bypass Grafting on Mortality

Ji-Hyun Chin, MD, PhD, Jun-Young Jo, MD, Eun-Ho Lee, MD, PhD[1], Wook-Jong Kim, MD, PhD, Dae-Kee Choi, MD, PhD, Ji-Yeon Sim, MD, PhD, Kyu Taek Choi, MD, PhD, In-Cheol Choi, MD, PhD

Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Objective: To evaluate the prognostic impacts of postoperative increases in serum amino transaminases on 1-year mortality in patients who underwent coronary artery bypass graft.
Design: A retrospective analysis.
Setting: A tertiary care university hospital.
Participants: A total of 1,950 patients who underwent coronary artery bypass graft.
Interventions: None.
Measurements and Main Results: Aspartate amino transaminase and alanine amino transaminase ratios were calculated as the ratio between the peak aspartate amino transaminase and alanine amino transaminase within the first 5 post-operative days and their respective upper limit of normal values. A ratio of 2.0 was seen to be the minimum for which a difference in 1-year mortality could be detected in univariate analysis, when considering simultaneously both aspartate amino transaminase and alanine amino transaminase ratios. Multivariable analysis showed an association between an aspartate amino transaminase ratio > 2.0 and increased 1-year mortality (hazard ratio [HR] 2.68, 95% confidence interval [CI] 1.42-5.05, P = 0.002), and also between both an aspartate amino transaminase and alanine amino transaminase ratio > 2.0 and increased 1-year mortality (HR 3.90, 95% CI 1.87-8.14, P < 0.001). However, increases in alanine amino transaminase only above the upper limit of normal were not associated with increased 1-year mortality.
Conclusions: Postoperative increases in aspartate amino transaminase only and increases in both aspartate amino transaminase and alanine amino transaminase greater than twice the upper limit of normal were associated with increased 1-year mortality in patients undergoing coronary artery bypass graft.

Key Words: coronary artery bypass graft; ventriculo-aortic junction; one-year mortality; postoperative alanine amino transaminase; postoperative aspartate amino transaminase

ASSESSMENT OF SERUM AMINO transaminase levels, including aspartate amino transaminase (AST) and alanine amino transaminase (ALT), has been used to detect liver diseases because AST and ALT are contained in hepatocytes.[1] Serum AST also has been identified as a cardiac enzyme, and evaluation of this can be used to diagnose myocardial infarction.[1,2] Aside from use as a marker of organ damage,

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[1]*Address reprint requests to* Eun-Ho Lee, MD, PhD, Associate Professor, Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul, 05505, Republic of Korea.
E-mail address: leho@naver.com (E.-H. Lee).

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increase in these enzymes has been reported to be associated with adverse outcomes in the general population.[3–6]

In the surgical settings, recent studies have shown that postoperative increase in serum amino transaminases may be related to postoperative outcomes in patients undergoing cardiac surgery.[2,7–9] Postoperative increase in AST was independently associated with both short- and long-term mortality following coronary artery bypass graft (CABG), irrespective of the presence of postoperative myocardial infarction.[2] However, previous studies did not differentiate between isolated increase in AST and simultaneous increase in both AST and ALT. It may be possible that the prognostic impacts of postoperative increase in serum amino transaminases may vary according to differences in individual amino transaminase changes when considering the possible differences in the underlying causes of these changes. Isolated increase in AST is more likely to reflect myocardial injury, and increase in both AST and ALT is more likely to indicate organ injury, including liver injury, caused by global hypoperfusion.

In this study, the authors aimed to investigate the effect of amino transaminase increase on 1-year mortality in patients who underwent CABG. Data were evaluated from three patient groups: (1) postoperative increase in AST only, (2) postoperative increase in ALT only, and (3) postoperative increase in both AST and ALT. The authors hypothesized that all 3 groups may be associated with the increased 1-year mortality, with postoperative increase in both AST and ALT potentially reflecting a higher mortality risk.

Methods

This retrospective observational study was conducted using data from patients who had undergone elective CABG between January 2006 and December 2012. Patients were excluded from the analysis if they showed a preoperative abnormal liver function test (defined as AST >40 IU/L, ALT >40 IU/L, total bilirubin >1.2 mg/dL, or alkaline phosphatase >120 IU/L), had preoperative liver cirrhosis, underwent CABG for reasons other than coronary artery ischemic disease, and had undergone combined valvular surgery with CABG. The research protocol was approved and the requirement of written informed consent was waived by the authors' Institutional Review Board (AMC IRB 2014-0381). Patient data including demographic information, comorbidities, laboratory data, medication use, postoperative management, and morbidity and mortality, were obtained from the Coronary Artery Bypass Surgery and Anesthesia Database of the authors' institution and from a retrospective review of electronic medical records.

Preoperative management, anesthesia, surgical technique, and postoperative management were standardized for all CABG patients at the authors' institution.[10] Postoperative laboratory assessment of serum AST and ALT was performed daily when patients were in the intensive care unit (usually for the first 3 postoperative days), after which assessment was performed on the second day in the general ward and twice weekly until discharge. Additional tests for serum AST and ALT were performed when necessary at the attending physician's discretion. Serum AST and ALT levels were measured using a Roche Cobas 8000 c702 analyzer (Roche Diagnostics, Germany) on the basis of the UV test. Postoperative serum AST was defined as the peak value within the first 5 postoperative days, and the AST ratio was calculated as the ratio between the peak AST and the upper limit of normal. Serum ALT levels and the ratio were determined in the same way.

The primary endpoint of the study was all-cause mortality within 1 year of CABG. The secondary endpoint was all-cause mortality within 90 days of CABG.

Statistical Analysis

Data were expressed as the median (interquartile range) or frequencies (percentages). Continuous variables were compared using a t test or Mann-Whitney U test for the parametric and nonparametric variables, respectively. Categorical variables were compared using a chi-square test or Fisher's exact test, as appropriate.

The areas under the receiver operating characteristic curves for AST and ALT to predict 1-year mortality were 0.62 and 0.54, respectively, implying poor discrimination performance in prediction of 1-year mortality. The cut-off values for the AST and ALT values to predict 1-year mortality were 78 IU/L and 38 IU/L, respectively; however, rather than use these values, the AST and ALT ratios were adopted rather than using cut-off values, as this study aimed to evaluate the prognostic effect of simultaneous increase in postoperative AST and ALT.

The 1-year survival rate according to the AST ratio and ALT ratio was evaluated using Kaplan-Meier estimates and compared using the log-rank test. The crude and adjusted risks of the AST ratio and ALT ratio for 1-year mortality were compared using univariate and multivariable Cox proportional hazard regression analyses, and hazard ratios (HRs) with 95% confidence intervals (CIs) calculated. For multivariable analysis, a ratio of 2.0 was selected, as this ratio was the minimum ratio that could detect a difference in 1-year mortality in the univariate analysis. All variables in Table 1 were examined, and variables with p values ≤ 0.10 in the univariate analyses (ie, body mass index, logistic EuroSCORE, hematocrit, albumin, cholesterol, C-reactive protein, ratio of early transmitral flow velocity to early diastolic mitral annulus velocity, pericardial effusion, statins, diuretic use, infused packed red blood cell, and postoperative AST ratio and ALT ratio) were entered into the multivariable analysis with a backward elimination process. Sensitivity analysis was undertaken by performing multivariable analyses, which included all the variables in the primary multivariable model plus postoperative cardiovascular sequential organ failure assessment (SOFAc) score obtained in the intensive care unit. In addition, the crude risks of the AST ratio and ALT ratio for 90-days mortality were compared using univariate Cox proportional hazard regression analyses. The proportion hazards assumption was confirmed by examining the log (-log[survival]) curves and by testing the Schoenfeld residuals, and no relevant violation was found.

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