Clinical Study

Is Leukocytosis a Predictor for Recurrence of Ischemic Events after Coronary Artery Bypass Graft Surgery? A Cohort Study

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Objective. Studies have shown that inflammation plays an important role in pathogenesis of coronary artery disease. The present study was designed to evaluate the role of high WBC count before CABG in predicting the risk of ischemic events after CABG.

Methods and Results. This prospective study was carried out on 380 patients who underwent CABG surgery. Ninety seven patients (25.5%) had recurrent ischemic event. Mean WBC count before CABG surgery in patients with recurrent ischemic event was 7267 mic/lit ± 1863, which was significantly higher than the others, with a mean WBC count of 6721 mic/lit ± 1734 (P = 0.011). Patients with a WBC count more than 6000 mic/lit were at the highest risk for recurrent ischemic event (OR = 2.11, 95% CI = 1.18–3.44, P = 0.009). After adjustment for age, sex, family history, smoking, hyperlipidemia, Logestic Euro score, post operative enzyme release (CK.mb), arterial graft and BMI, the relationship between the group with WBC count higher than 6000 mic/lit and recurrent of ischemic event remained significant (OR = 2.25, 95% CI = 1.2 to 4, P = 0.005). Conclusions. High WBC count before CABG surgery is an independent risk factor for ischemic events one year after the surgery.

1. Introduction

Inflammation plays a significant role in progression and pathogenesis of coronary artery disease [1]. Several studies have shown an association between high white blood cell (WBC) count and progression of coronary artery disease (CAD) [2, 3]. Leukocytosis also increases long-term mortality in patients with CAD. For the first time, the association between leukocytosis and CAD was described by Friedman et al. [2] Various factors affect the prognosis of coronary artery bypass graft (CABG) surgery [4, 5]. Inflammatory factors such as C reactive protein (CRP) level before CABG has been described as one of these factors [6]. Limited studies has suggested leukocytosis as one of the prognostic factors for in-hospital mortality after CABG [7]. Leukocytosis may also increase mortality following CABG surgery [8]. However, no study has investigated the role of high WBC count in increasing the risk of recurrent ischemic event after CABG surgery. In this study we investigated the role of WBC count before surgery in predicting the risk of recurrent ischemia after surgery.

2. Method and Materials

The study was carried out from October 2004 to January 2007 and the study protocol was approved by the ethics committee of Tabriz University of Medical Sciences. Studied population included all patients who were hospitalized in Shahid Madani Heart Center in Tabriz, Iran for elective CABG surgery. After signing a consent form, all patients were interviewed, using a structured questionnaire, by a trained staff physician. Collected data included age, gender, anthropometrics data, history of hypertension, diabetes, smoking, cardiac surgery, chronic obstructive pulmonary disease,
ejection fraction prior to the surgery and the number of significantly involved arteries in angiography. Surgical data including the surgical method (on pump or off pump), number of grafts, duration of pump attachment, and duration of the surgery were recorded after the surgery.

Patients older than 70 years old or patients with a history of MI in the past three months, history of infection, trauma, gastrointestinal bleeding or surgery a week before the surgery, history of malignancy in the past three years, and an ejection fraction less than 30% were excluded. Out of 422 patients, 42 patients meet the exclusion criteria and a total of 380 patients were included in the study and were followed for one year.

After obtaining written informed consent, blood sample of each included patients was drawn and sent to laboratory for complete blood count (CBC), cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), blood urea (BUN), and creatinin (Cr) levels in standard situation.

### 3. Followup

Patients were followed for one year after the surgery. In-hospital followup included obtaining information regarding in-hospital mortality and postsurgical complications such as any need for intra-aortic balloon pump, ventricular fibrillation (VF), atrial fibrillation (AF), ischemic symptoms, severe post surgical bleeding, acute myocardial infarction (MI), infection and incidence of neurological complications during post-surgical hospital course. One year after the surgery, patient or the family (in case of patient's death) was contacted with phone or in person. To prevent bias, patients were followed by the same group of investigators who had interviewed the patient initially and were also blind to the result of the laboratory tests.

In followup contact, the patients were investigated regarding the overall mortality and morbidity due to cardiac causes, incidence of recurrent ischemic events or new onset cerebrovascular accident (CVA). Recurrent of ischemic event was defined as a new onset MI, unstable angina leading to hospitalization, stable angina, or revascularization (PTCA or CABG) after the initial surgery. Stable angina was defined as the occurrence of typical chest pain. Chest pain was considered to be typical when any of the following criteria were met: (1) pain in exercise, (2) retrosternal chest pain, or (3) remedy with resting or taking sublingual TNG. Mortality from cardiac origin was defined as sudden cardiac death or death in hospital following hospitalization because of MI or unstable angina (U/A). Patients who were hospitalized because of resting chest pain or chest pain with minimum exercise included in the U/A category. In addition, patients who met any two of the following three criteria were regarded to have MI: (1) chest pain longer than 30 minutes, (2) ST segment elevation, and (3) elevated cardiac enzymes.

### 4. Statistic Analysis

SPSS 11.5 statistical software package (SPSS Inc., Chicago, IL) was used in statistical analysis. Statistical significance was set at $P \leq 0.05$. The distribution of age, sex, laboratory values, and body mass index (BMI), were analyzed by means and standard deviation for categorical variables. Chi-square test was used to find whether patients who had recurrent ischemic events were different in regards to the presence of leukocytosis before surgery.

To estimate and adjust for confounding variable, multivariable stepwise forward and backward logistic regression tests were used. For multivariate analysis, we entered all risk factor for recurrence of ischemic events and all covariates with $P < 0.05$ on univariate analysis. Student $t$-test was used to compare the mean of WBC count, age, BMI, and ejection fraction in patients with or without recurrent event.

### 5. Results

After applying inclusion and exclusion criteria, 380 patients were included in statistical analysis. Two hundred eighty one patients (73.9%) were male and 99 (26.1%) were female. Mean age of the patients was 57 years old (Table 1). Overall, 97 (25.5%) patients had recurrent ischemic event. The difference between the mean WBC count in patients with and without a recurrent ischemic event was significant ($7267 \text{ mic/lit} \pm 1863$ versus $6721 \text{ mic/lit} \pm 1734$) ($P = 0.011$). Thirty days followup showed that the patients with WBC

### Table 1: Base line characteristics of the studied population.

| Total number | 380 |
|-------------|-----|
| Male gender | 281 (73.9%) |
| Mean age | 57 ± 9.4 |
| WBC count | |
| ≥6000 mic/lit | 253 (66.6%) |
| Hypertension | 211 (55.5%) |
| Diabetes mellitus | 49 (12.9%) |
| Smoker | 162 (42.6%) |
| Family history | 113 (29.7%) |
| BMI ≥ 29 kg/m² | 103 (27%) |
| Cholesterol | |
| <200 | 234 (61.6%) |
| 200–240 | 79 (20.6%) |
| >240 | 67 (17.6%) |
| Ejection fraction (%) | |
| <40 | 84 (22.1%) |
| 40–50 | 158 (41.6%) |
| >50 | 138 (36.3%) |
| Left main > 50% | 34 (8.9%) |
| LAD > 70% | 342 (90%) |
| 2VD | 112 (29.5%) |
| 3VD | 171 (45%) |
| Cr > 1.5 mg/dL | 18 (0.04%) |
| Off pump | 205 (53.9%) |
| On pump | 175 (46.1%) |
| Mean pump time | 45 min |

WBC: White Blood Cell; BMI: Body Mass Index; 2VD: 2 Vessel Disease.
not any difference in recurrent ischemic events in patient with “on-pump” and “off-pump” method, ($P = 0.53$). The difference of pump timing between the patients with and without recurrent events was not significant (100.07/min versus 99.5/min, $P = 0.59$). Overall, the mean graft number was 2.5. Patients with and without recurrent events did not have significant difference in regard to the graft number ($P = 0.38$).

6. Discussion

This study shows that elevated WBC count, after elective CABG surgery, is an independent risk factor for recurrent ischemic event one year after the surgery. The significance of elevated WBC, as a risk factor for recurrent ischemic event, stayed the same in multivariate analysis. To the best of our knowledge, our study is the only study which evaluated the effect of elevated WBC count after CABG and the risk of ischemic event one year after the surgery. Because of the relatively small sample size, we were not able to have a precise evaluation of elevated WBC and one-year mortality.

Our study is well in accordance to the others and supports the role of inflammatory factors in prognosis of coronary artery disease. The role of elevated WBC count and coronary artery disease risk had been discussed previously [9, 10]. Our result is also in accordance with the findings of others which have showed the effect of elevated WBC count after CABG on postoperative mortality and early and late complications [7, 11, 12]. The relationship between increased WBC count and early postoperative complications such as stroke and necessitation of intra-aortic pump have been reported [12]. In another study, the role of WBC before CABG on increased rate of inpatient mortality and also mortality one year following the surgery was studied but the study did not evaluate the role of WBC on recurrent ischemia.

The effect of neutrophils on myocardial function after MI and its effects on early postmyocardial infarction CHF have been studied [13]. Neutrophils and macrophages can cause myocardial reperfusion injury [14]. The effect of other acute phase reactants such as TNF, CRP and IL6 in prognosis of acute coronary syndromes is also known [15, 16]. The role of CRP, in atherosclerosis and its effects on patients’ prognosis and mortality after CABG have been investigated [17–20]. The impact of elevated WBC before surgery on preoperative myocardial necrosis, inpatient mortality, and mortality one year after the surgery has also been shown.
Table 4: Sensitivity, specificity, and positive and negative predictive values also area under the ROC curve for quantitative variable.

| Variable                  | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | PPV (%) (95% CI) | NPV (%) (95% CI) | AUC ± SD, P Value |
|---------------------------|--------------------------|--------------------------|------------------|------------------|-------------------|
| WBC                       |                          |                          |                  |                  |                   |
| ≥6000 mic/lit             | 77 (67–84)               | 37 (31–43)               | 29 (24–35)       | 82 (74–88)       | 0.58 ± 0.033, P = 0.016 |
| HTN                       | 63 (54–72)               | 47 (41–54)               | 33 (27–40)       | 76 (69–83)       |                   |
| Family history            | 32 (23–43)               | 71 (65–76)               | 28 (21–38)       | 74 (68–79)       |                   |
| DM                        | 16 (9–24)                | 88 (83–91)               | 32 (20–47)       | 74 (69–79)       |                   |
| Smoking                   | 48 (38–57)               | 59 (53–65)               | 32 (25–39)       | 74 (67–79)       |                   |
| BMI ≥ 29 kg/m²            | 40 (30–50)               | 77 (72–82)               | 40 (31–50)       | 77 (71–81)       | 0.55 ± 0.035, P = 0.1 |

PPV: Positive Predictive Value; NPV: Negative Predictive Value; WBC: White Blood Cell; BMI: Body Mass Index.

Table 5: Univariate analysis.

| Variable                  | Ischemic event | No ischemic event | OR (95% CI) | P value |
|---------------------------|----------------|-------------------|-------------|---------|
| Sex (male)                | 83 (69.7%)     | 198 (75.9%)       | 1.36 (0.84–2.21) | 0.208   |
| Mean age                  | 57.09 (±9.4)   | 57.7 (±9.4)       | 0.51        |         |
| HTN                       | 71 (59.7%)     | 140 (53.6%)       | 1.27 (0.82–1.98) | 0.27    |
| Smoker                    | 52 (50.7%)     | 110 (42.1%)       | 1.065 (0.68–1.65) | 0.77    |
| WBC                       |                |                   |             |         |
| ≥6000 mic/lit             | 92 (77.3%)     | 161 (61.7%)       | 2.11 (1.28–3.44) | 0.003   |
| Left main >50%            | 13 (10.9%)     | 21 (8%)           | 1.402 (0.67–2.89) | 0.015   |
| LAD >70%                  | 106 (89.1%)    | 236 (91%)         | 0.79 (0.38–1.62) | 0.52    |
| Ejection fraction         |                |                   |             |         |
| 40%–50%                   | 51 (40.2%)     | 107 (42.3%)       | 0.84 (0.48–1.48) | 0.55    |
| >50%                      | 49 (38.6%)     | 89 (32.2%)        | 0.83 (0.46–1.47) | 0.52    |
| Family history            | 33 (27.7%)     | 80 (30.7%)        | 0.86 (0.53–1.4)  | 0.56    |
| Number of graft (mean)    | 2.5 (±0.91)    | 2.58 (±0.82)      | 0.38        |         |
| Cr > 1.5 mg/dL            | 8 (6.7%)       | 10 (12.4%)        | 1.809 (0.69–4.7) | 0.21    |
| Pump timing (mean)/min    | 43.73 min      | 46.91 min         | 0.59        |         |
| CPB (mean)/min            | 243/4 (±91)    | 243 (±86)         | 0.98        |         |
| CK.MB                     | 47 (±41)       | 43 (±25)          | 0.4         |         |
| Logistic EuroScore        | 2.61 (±1.3)    | 2.2 (±1.2)        | 0.01        |         |
| Arterial graft            | 85 (87.6%)     | 246 (86.9%)       | 1.06 (0.53–2.1) | 0.85    |
| ASA                       | 94 (96.9%)     | 273 (96.5%)       | 1.1 (0.3–4.2)  | 0.83    |
| Beta.blocher              | 79 (81.4%)     | 220 (77.3%)       | 1.2 (0.7–2.2)  | 0.41    |
| Ace.Inh                   | 46 (47.4%)     | 149 (52.7%)       | 0.81 (0.5–1.2)  | 0.37    |
| CCB                       | 11 (11.3%)     | 34 (12%)          | 0.93 (0.45–1.9) | 0.85    |
| Statin                    | 61 (62.9%)     | 150 (53%)         | 1.5 (0.9–2.4)  | 0.09    |
| Diuretic                  | 6 (6.2%)       | 14 (4.9%)         | 1.27 (0.43–3.3) | 0.63    |
| Nitriglicerin             | 30 (30.9%)     | 72 (25.4%)        | 1.3 (0.79–2.1) | 0.29    |

BMI: Body Mass Index; WBC: White Blood Cell; LAD: Left Anterior Descending; CCB: calcium channel blocker.

Probably, increased use of intra-aortic balloon pump during hospitalization is linked to elevated WBC count before surgery [11].

Recently, in a large multicenter double-blind study, 1273 patients who underwent CABG were followed for up to 11 years and the effect of hematologic elements and WBC in post-CABG prognosis was evaluated [12]. Increase WBC count was associated with poorer prognosis after CABG but this association was not related to the other parameters such as hematocrit or platelet count. There are some studies which have described the role of CRP in direct vascular injury as a preinflammatory and prothrombotic factor, mainly through
Table 6: Multivariable analysis and adjusted odds ratio.

| Variable                  | OR (before adjust) | OR (after adjust) | P value (after adjust) |
|---------------------------|--------------------|-------------------|------------------------|
| WBC ≥6000 mic/lit         | 2.11 (95% CI = 1.28–3.44) | 2.25 (95% CI = 1.2–4) | 0.005                 |
| Hypertension              | 1.27 (95% CI = 0.82–1.98)  | 1.17 (95% CI = 0.72–1.907) | 0.54                |
| Smoking                   | 1.065 (95% CI = 0.68–1.65) | 1.07 (95% CI = 0.64–1.7) | 0.42                |
| Diabetes mellitus         | 1.07 (95% CI = 0.56–2.03)  | 0.89 (95% CI = 0.39–1.6) | 0.56                |
| Age                       | 0.99 (95% CI = 0.97–1.01)  | 0.97 (95% CI = 0.94–1.8) | 0.83                |
| BMI ≥ 29                  | 1.79 (95% CI = 1.11–2.89)  | 2.007 (95% CI = 1.15–3.47) | 0.013             |
| Family history            | 0.86 (95% CI = 0.53–1.4)   | 1.05 (95% CI = 0.62–1.8) | 0.82                |

Cholesterol

| Variable                  | OR (before adjust) | OR (after adjust) | P value (after adjust) |
|---------------------------|--------------------|-------------------|------------------------|
| 200–240                   | 1.16 (95% CI = 0.68–2) | 0.8 (95% CI = 0.43–1.5) | 0.79                |
| >240                      | 0.95 (95% CI = 0.52–1.73) | 1.01 (95% CI = 0.56–2.1) | 0.97                |
| Waist circumference       | 1.05 (95% CI = 0.68–1.62) | 1.01 (95% CI = 0.58–1.7) | 0.97                |
| (Male > 102 cm and female > 88 cm) | 1.809 (95% CI = 0.69–0.47) | 0.95 (95% CI = 0.31–2.8) | 0.93                |
| Cr > 1.5 mg/dL            | 1.22 (95% CI = 1.03–1.4)  | 1.07 (95% CI = 1.1–1.6) | 0.002               |
| Euro score                | 0.97 (95% CI = 0.47–1.9)  | 1.07 (95% CI = 0.51–2.2) | 0.84                |
| Arterial graft            | 0.91 (95% CI = 0.98–1.005) | 0.99 (95% CI = 0.98–1.004) | 0.28                |

It seems that elevated white blood cell count has a good association with the recurrent ischemic events after CABG. Probably patients with elevated WBC count, before CABG, would get more benefit from aggressive cardiovascular risk modification.

8. Study Limitations

Although all samplings were done in five days before the surgery, sampling time was not the same in all patients. Therefore different sampling time might have some influence on our results. We did not check white blood cell count after surgery. We did not do angiography to find whether recurrent ischemic events were due to restenosis of grafted vessels or not. It was better that patients undergo angiography to determine cause of recurrent ischemia. Small population and short followup time of patients are another limitation.

Conflict of Interests

The authors declared that they have no conflict of interest.

References

[1] R. Rose, "Atherosclerosis and inflammatory disease," *The New England Journal of Medicine*, vol. 340, pp. 115–126, 1999.
[2] G. D. Friedman, A. L. Klatsky, and A. B. Siegelaub, “Letter: leukocyte count and myocardial infarction: correction,” *The New England Journal of Medicine*, vol. 291, no. 25, p. 1361, 1974.
[3] E. G. Bovill, D. E. Bild, G. Heiss et al., “White blood cell counts in persons aged 65 years or more from the cardiovascular health study: correlations with baseline clinical and demographic characteristics,” *American Journal of Epidemiology*, vol. 143, no. 11, pp. 1107–1115, 1996.
[4] European Coronary Surgery Study Group, “Long-term results of prospective randomised study of coronary artery bypass surgery in stable angina pectoris,” The Lancet, vol. 2, no. 8309, pp. 1173–1180, 1982.

[5] S. Yusuf, D. Zucker, P. Peduzzi et al., “Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration,” The Lancet, vol. 344, no. 8922, pp. 563–570, 1994.

[6] D. Milazzo, L. M. Biasucci, N. Luciani et al., “Elevated levels of C-reactive protein before coronary artery bypass grafting predict recurrence of ischemic events,” The American Journal of Cardiology, vol. 84, no. 4, pp. 459–461, 1999.

[7] L. J. Dacey, J. DeSimone, J. H. Braxton et al., “Preoperative white blood cell count and mortality and morbidity after coronary artery bypass grafting,” Annals of Thoracic Surgery, vol. 76, no. 3, pp. 760–764, 2003.

[8] N. Newall, A. D. Grayson, A. Y. Oo et al., “Preoperative white blood cell count is independently associated with higher perioperative cardiac enzyme release and increased 1-year mortality after coronary artery bypass grafting,” Annals of Thoracic Surgery, vol. 81, no. 2, pp. 583–590, 2006.

[9] F. Haverkate, S. G. Thompson, S. D. M. Pyke, J. R. Gallimore, and M. B. Pepys, “Production of C-reactive protein and risk of coronary events in stable and unstable angina,” The Lancet, vol. 349, no. 9050, pp. 462–466, 1997.

[10] H. S. Gurm, D. L. Bhatt, A. M. Lincoff et al., “Impact of preprocedural white blood cell count on long term mortality after percutaneous coronary intervention: insights from the EPIC, EPILOG, and EPISTENT trials,” Heart, vol. 89, no. 10, pp. 1200–1204, 2003.

[11] N. E. Nil, G. Antony, and Y. Auny, “Preoperative white blood cell Count is independently associated with higher perioperative cardiac enzyme release and increased 1-year mortality after Coronary artery bypass grafting,” Annals of Thoracic Surgery, vol. 81, pp. 583–590, 2006.

[12] K. J. Mukamal, G. A. Wellenius, and M. A. Mittleman, “Hematologic parameters, atherosclerotic progression, and prognosis in patients with previous coronary artery bypass grafting (from the Post CABG Trial),” The American Journal of Cardiology, vol. 103, no. 3, pp. 328–332, 2009.

[13] F. Rashidi, A. Rashidi, A. Golmohamadi et al., “Does absolute neutrophilia predict early congestive heart failure after acute myocardial infarction? A cross-sectional study,” Southern Medical Journal, vol. 101, no. 1, pp. 19–23, 2008.

[14] J. E. Jordan, Z. Q. Zhao, and J. Vinter-Johansen, “The role of neutrophils in myocardial ischemia—reperfusion injury,” Cardiovascular Research, vol. 43, no. 4, pp. 860–878, 1999.

[15] G. Liuzzo, L. M. Biasucci, J. R. Gallimore et al., “The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina,” The New England Journal of Medicine, vol. 331, no. 7, pp. 417–424, 1994.

[16] P. M. Ridker, N. Rifai, M. Pfeffer, F. Sacks, S. Lepage, and E. Braunwald, “Elevation of tumor necrosis factor-α and increased risk of recurrent coronary events after myocardial infarction,” Circulation, vol. 101, no. 18, pp. 2149–2153, 2000.

[17] O. P. Kangasniemi, F. Biancari, J. Luukkonen et al., “Preoperative C-reactive protein is predictive of long-term outcome after coronary artery bypass surgery,” European Journal of Cardio-thoracic Surgery, vol. 29, no. 6, pp. 983–985, 2006.

[18] F. Biancari, J. Lahtinen, S. Lepojärvi et al., “Preoperative C-reactive protein and outcome after coronary artery bypass surgery,” Annals of Thoracic Surgery, vol. 76, no. 6, pp. 2007–2012, 2003.

[19] T. Palmerini, A. Marzocchi, C. Marrozzini et al., “Preoperative C-reactive protein levels predict 9-month mortality after coronary artery bypass grafting surgery for the treatment of left main coronary artery stenosis,” European Journal of Cardio-thoracic Surgery, vol. 31, no. 4, pp. 685–690, 2007.

[20] M. Gaudino, G. Nasso, F. Andreotti et al., “Preoperative C-reactive protein level and outcome following coronary surgery,” European Journal of Cardio-thoracic Surgery, vol. 22, no. 4, pp. 521–526, 2002.

[21] S. P. Ballou and G. Lozanski, “Induction of inflammatory cytokine release from cultured human monocytes by C-reactive protein,” Cytokine, vol. 4, no. 5, pp. 361–368, 1992.

[22] R. F. Salamonsen, J. Anderson, M. Anderson, M. Bailey, G. Magrin, and F. Rosenfeldt, “Total leukocyte control for elective coronary bypass surgery does not improve short-term outcome,” Annals of Thoracic Surgery, vol. 79, no. 6, pp. 2032–2038, 2005.

[23] J. F. Gott, W. A. Cooper, F. E. Schmidt Jr. et al., “Modifying risk for extracorporeal circulation: trial of four anti-inflammatory strategies,” Annals of Thoracic Surgery, vol. 66, no. 3, pp. 747–754, 1998.

[24] J. Sawa and H. Matsuda, “Myocardial protection with leukocyte depletion in cardiac surgery,” Seminars in Thoracic and Cardiovascular Surgery, vol. 13, pp. 73–81, 2000.

[25] H. B. Hubert, M. Feinleib, P. M. McNamara, and W. P. Castelli, “Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study,” Circulation, vol. 67, no. 5, pp. 968–977, 1983.

[26] R. Wolk, P. Berger, R. J. Lennon, E. S. Brilakis, and V. K. Somers, “Body mass index: a risk factor for unstable angina and myocardial infarction in patients with angiographically confirmed coronary artery disease,” Circulation, vol. 108, no. 18, pp. 2206–2211, 2003.

[27] A. Romero-Corral, V. M. Montori, V. K. Somers et al., “Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies,” The Lancet, vol. 368, no. 9536, pp. 666–678, 2006.
