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ORIGINAL ARTICLES

Predictors associated with stroke after coronary artery bypass grafting in Turkish population

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Abstract

Background Objective: Postoperative stroke is a serious adverse event, a major cause of morbidity and mortality after coronary artery bypass grafting (CABG). This study is designed to determine the incidence of stroke after CABG and to identify the preoperative, intraoperative and postoperative risk factors associated with the development of a stroke. *Methods:* Between January 2019 and December 2022, 1.555 CABG were performed. Retrospective analysis of the patient files revealed that 24 (1.48%) patients had stroke in the postoperative period. Variables were compared with patients without neurological deficits (n=50) who had undergone CABG. Predictors of preoperative, intraoperative and postoperative stroke were identified. *Results:* The incidence of postoperative stroke was 1.48% (n=24). Mean age of these patients was 63.86 ± 8.58 years, and 59 (79.7%) were males. Chronic renal failure (p= 0.011), previous CABG (p=0.009), carotid artery disease (p=0.009), CRP levels (p=0.004) and Monocyte/Lymphocyte ratio (p=0.019) were identified as important preoperative risk factors for stroke development but there were no diffirence prevalence of age, sex, diabetes, hypertension, congestive heart failure and atrial fibrillation.
Conclusion: Five variables (chronic renal failure, prior CABD, prior carotid artery disease, preoperative CRP levels and Monocyte/Lymphocyte ratio were found as risk factors for stroke after CABG. The development of postoperative stroke is associated with multiple morbidities and increased mortality. Careful assessment and management of risk factors should be implemented to reduce this important complication after CABG.

Keywords: Coronary artery disease, cerebrovascular stroke, risk factor

INTRODUCTION

Stroke is a major cause of morbidity and mortality after coronary artery bypass grafting (CABG).[1] The incidence of stroke after CABG was 1.1–5.7%. About 37–59% of strokes occurred early.[2,3] Postoperative stroke also remains a catastrophic and costly complication of CABG, with a reported 21% mortality and mean hospital stay of 25 days among the survivors.[4] This mandates that additional interventions be developed in an attempt to decrease the incidence of stroke after coronary revascularization.[5] In literature the most important risk factors for CABG-associated stroke include advanced age, prior cerebrovascular disease, prior carotid artery stenosis, prior peripheral vascular disease, prolonged cardiopulmonary bypass time and postoperative atrial fibrillation.[1,6]

Knowledge of those at the highest risk of stroke after CABG could help to determine the most appropriate preoperative evaluation, identify therapeutic measures to reduce postoperative strokes and improve postoperative management.[1] The aim of the present study were to determine the incidence of stroke after CABG and to identify the preoperative and postoperative risk factors associated with the development of a stroke.

METHODS

Adult patients aged ≥18 years who underwent an isolated CABG procedure utilizing cardiopulmonary bypass (CPB) at either Lokman

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Hekim Univercity Akay Hospital between January 2019 and December 2022, were included in this retrospective study sample (n=1555). Our Institutional Research Review Board approved this study. Among them, 24/1555 (1.48%) patients, with no history of previous cerebrovascular events, suffered postoperative stroke and diagnosed by computerized tomography (CT) or magnetic resonance imaging (MRI). MRI was done on a 1.5 Tesla scan, CT was done on a 64-section CT scan.

The data included demographic, perioperative clinical and laboratory variables and the postoperative stroke features. A control group was formed to identify predictors of neurological complications. The control group consisted of 50 cardiac surgery patients without neurological complications selected according to age, gender and type of intervention.

A postoperative stroke was defined as a permanent new neurologic deficit occurring within 24 hours after operation. Some variables were evaluated in this study. Demographic and preoperative variables included age, sex, priority of surgery (elective, urgent, and emergent), prior myocardial infarction, preoperative carotid artery disease, hypertension, diabetes mellitus, dyslipidemia, renal failure, prior cardiac surgery, ventricular arrhythmias and cardiac ejection fraction. Of the postoperative variables, only atrial fibrillation was evaluated.

Statistical analysis

Descriptive statistics for variables were calculated as follows: frequency and percentages for qualitative variables, and arithmetic mean and standard deviation for quantitative variables. Parametric test assumptions were checked for the data. The Shapiro-Wilk test was applied to investigate the normality of distribution for quantitative variables. Nonparametric hypothesis tests were performed accordingly. Two independent groups were compared using the Mann-Whitney U test. Chi-square tests (Pearson Chi-Square and Fisher's Exact test) were used to investigate the statistical significance of associations between qualitative variables. The level of significance was set at 0.05. All calculations were performed with SPSS (Version 26.0 for Mac).

RESULTS

Between 2019 and 2022, 24 of 1,555 patients who underwent bypass were diagnosed with ischemic stroke (1.48%). The mean age was 63.86 ± 8.58 years, and 59 (79.7%) were males. Postoperative stroke was defined as a postoperative neurological deficit lasting more than 24 hours and associated with evidence of a brain lesion on CT or MRI.

When stroke and No stroke cohorts were compared, no difference was found in terms of age and gender. Stroke cohort mean age was 66.21 ± 8.34 years, and 20/24 (83.3%) were male. Besides, about 50% of strokes occurred early (intraoperatively).

The stroke cohort also tended to have a higher comorbidity burden of chronic renal failure (p= 0.011), previous CABD (p=0.009) and carotid artery disease (p=0.009) but there were no diffirence prevalence of diabetes, hypertension, congestive heart failure and atrial fibrillation. Preoperative, intraoperative and postoperative data in patients with and without stroke after bypass operation are summarized in Table 1.

The probability of developing postoperative stroke in patients with emergency CABG was not different from non-emergency patients. Off-pump CABG was performed in all of the stroke patients (70.8% vs 50%). Intraoperative support device or balloon pump was used in only one patient in the stroke group (4.2%).

Multi-vessel coronary revascularisation, concomitant heart valve procedures (70.8% vs 8%) and numbers of vessels grafted were similarly in both cohorts. In terms of operative characteristics were seen in Table 1.

The perioperative laboratory and Inflammation paramaters of groups were summarized in Table 2,3. Preoperatively, CRP level was 19.67 ± 23.96 vs. 7.76 ± 11.60 (p=0.004) and Monocyte/ Lymphocyte ratio was 0.37 ± 0.16 vs 0.27 ± 0.11 (p=0.019) in those with and without strokes, respectively. Other parameters were similar in the two groups.

Radiological examinations were done all of the stroke cohort. All of the stroke (n=24) patients had imaging evidence of ischemic stroke. Anterior system involvement was demonstrated in 7/24 people (29.2%), posterior system involvement was demonstrated in 5/24 (20.8%), and both systems were demonstrated in 12/24 (50.0%) with MR imaging. Ischemic stroke was single area in 4/24 (16.7%) patients and multiple areas in 20/24 (83.3%) patients.

Postoperative new-onset atrial fibrillation occurred in 29.2% of the patients who developed postoperative stroke and in 32% of the patients No stroke (p=0.805). Clinical evaluation was done with National Institutes of Health Stroke Scala (NIHSS). 4 patients had high NIHSS (>10)

Table 1: Preoperative, intraoperative and postoperative data for CABG-stroke patients and No stroke patients

Variables	CABG-No stroke (n=50)	CABG-stroke (n=24)	P value
Age (years), mean ±SD	62.74 ± 8.75	66.21 ± 8.34	0.119
Sex (Male)	39 (78%)	20 (83.3%)	0.761
Hypercholesterolemia	32 (64%)	19(79.2%)	0.187
Hypertension	25 (50%)	13 (54.2%)	0.737
Diabetes mellitus	16 (32%)	7 (29.2%)	0.805
Coronary artery disease	31 (62.0%)	16 (66.7%)	0.696
Chronic renal failure	3 (6%)	7 (29.2%)	**0.011**
Myocardial infarction	25 (%50)	17(%70.8)	0.090
Carotid artery disease	5 (10.0%)	9 (37.5%)	**0.009**
Preoperative AF	1 (2.0%)	2 (8.3%)	0.244
Prior cardiac surgery	0 (0%)	4 (16.7%)	**0.009**
Left ventricular ejection fraction (EF)	51.12 ± 13.77	54.18 ± 11.83	0.452
>55%	32 (64.0%)	14 (58.4%)	
45-54%	10 (20.0%)	2 (8.3%)	0.157
<44%	8 (16%)	8 (33.3%)	
CABG+valve operations	4(8%)	6(25%)	0.068
Mitral valve	3	5	
Aortic valve	1	0	NA
Mitral+Aortic valve	0	1	
İABP	0 (0.0%)	1 (4.2%)	0.324
Urgent operation	25 (50.0%)	17 (70.8%)	0.090
CABG-on pump	43 (86.0%)	24 (100.0%)	0.088
CABG-off pump	7 (14.0%)	0 (0.0%)	
CABG number oft grafts	3.18 ± 0.75	3.00 ± 0.83	0.320
Graft			
SVG	16 (32.0%)	9 (37.5%)	0.640
LİMA+SVG	34 (68.0%)	15 (62.5%)	
Postoperative AF	16 (32.0%)	7 (29.2%)	0.805
Exitus	1 (2.0%)	3 (12.5%)	0.097

Data are presented as mean ±SD unless indicated otherwise.
AF:Atrial Fibrillation, İABP: İntraaortic Balloon Pump, SVG: Saphenous Vein Graft, LiMA:Left internal Mammarian Artery

and 3 of these patients died. All cause mortality was 12.5% in the stroke cohort vs 2% in the No stroke cohort (p=0.097).

DISCUSSION

The purpose of this examination was to evaluate the predictors of perioperative, intraoperative and postoperative stroke after CABG. We evaluated the incidence of postoperative stroke in 1555 consecutive cardiac surgery patients, and found that 1.48% patients had neurological deficits. Ranjit et al.[5] found the incidence of stroke to be 1.4% and Frye and associates[7] found 1.9% during the initial hospitalization for surgery in the Coronary Artery Surgery Study experience.

Table 2: Preoperative laboratory variables

Variables	CABG-No stroke (n=50)	CABG-stroke (n=24)	P value
Urea, mean ±SD	34.17 ±12.10	45.01±25.64	0.161
Creatinine	0.94 ± 0.24	1.02 ± 0.33	0.358
Glomerular Filtration Rate (GFR)	83.28 ±18.36	77.09 ± 20.94	0.255
White blood cell count ($\times10^3/\mu L$)	9.74 ± 2.88	9.27 ± 2.93	0.463
Neutrophil count ($\times10^3/\mu L$)	6.52 ± 2.33	5.96 ± 2.41	0.299
Lymphocyte count ($\times10^3/\mu L$)	2.56 ± 1.13	2.31 ± 0.82	0.393
Monocyte count ($\times10^3/\mu L$)	0.66 ± 0.21	0.79 ± 0.30	0.095
Low-density lipoprotein cholesterol (mg/dl)	127.87 ± 55.20	133.56 ± 35.84	0.507
High density lipoprotein-cholesterol (mg/dl)	40.80 ± 9.96	41.25 ± 8.55	0.478
Triglyceride (mg/dl)	240..70 ± 259.48	199.50 ± 111.25	0.931
Troponin	3.24 ± 6.26	4.08 ± 7.61	0.849
High sensitivity c-reactive protein (mg/dl)	7.76 ± 11.60	19.67 ± 23.96	**0.004**

In contrast, Roach and colleagues[4] reported the incidence of adverse cerebral outcomes after CABG to be 6.1%. These differences in stroke incidence are due to the fact that CABG is performed by different physicians on different patient populations in various hospitals.

The etiology of postoperative stroke in CABG patients is multifactorial, with embolism as the predominant cause, while intraoperative hypotension and hemorrhage are less frequent.[3,8] In this study all patients strokes were ischemic, no hemorragia was observed.[2,9]

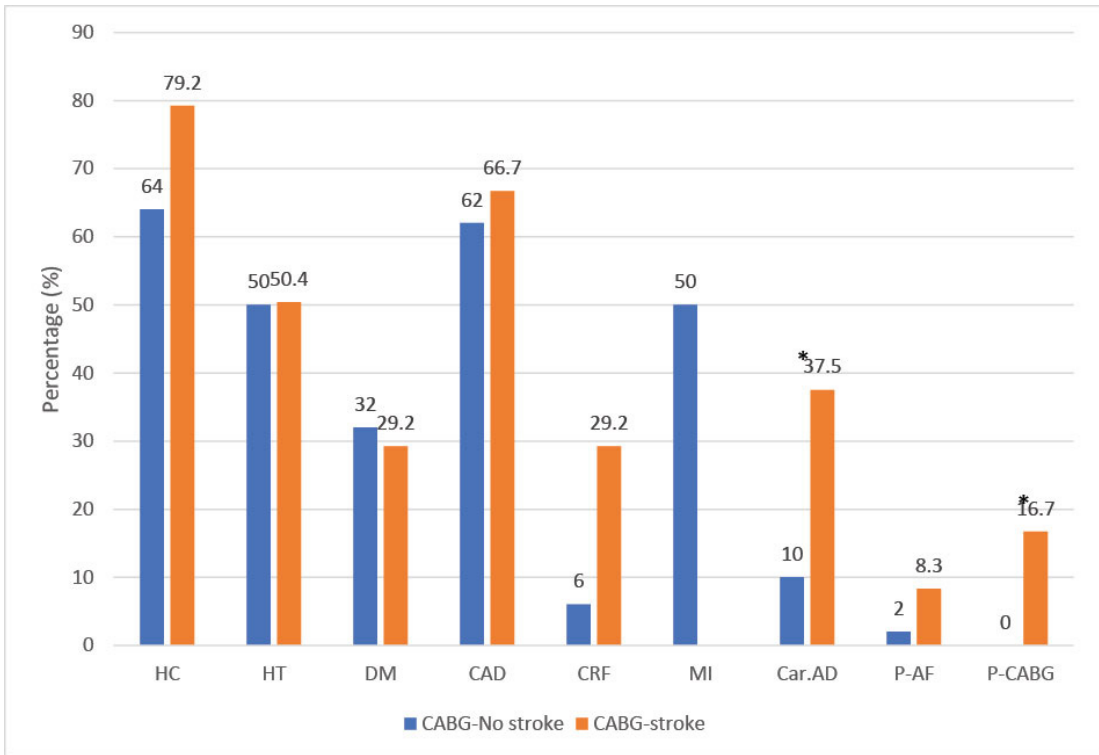
Several risk factors have all been identified to account for the early and delayed incidence of postoperative stroke.[10,11] Comorbid conditions, such as chronic renal insufficiency, previous cerebrovascular accident, carotid artery disease, hypertension, diabetes mellitus, advanced age and depressed ejection fraction, have been found in previous studies to predict postoperative stroke.[12] In this study several perioperative risk factors associated with the development of a postoperative stroke were identified. Prior CABG, prior carotid artery stenosis and chronic renal failure were found to be the most consistent independent perioperative predictors of stroke after CABG. No association was found with hypercholesterolemia, prior myocardial infarct, hypertension, diabetes mellitus, congestive heart failure and atrial fibrillation. New-onset atrial fibrillation and low cardiac output syndrome was associated with a higher risk of postoperative stroke in recently literatures[5], but in this study, no relationship was found with postoperative risk factors (Figure 1).

The most common mechanism of stroke following CABG is related to emboli originating from the ascending aorta during cross-clamping, cannulation, and creation of proximal anastomoses; however, intracardiac thrombi, hypoperfusion, and air emboli have all been implicated as possible. Pathological examination by Moody *et al*.[13] of the brain after conventional CABG revealed the presence of multiple emboli lodged in small cerebral arterioles and capillaries.[12] In this study, the rate of multiple embolism detected in MRI was high (83.3%), which supports the literature.

All laboratory parameters of the patients were checked before the operation. Only CRP and

Table 3: Inflammation paramaters of groups

Variables	CABG-No stroke	CABG-stroke	P value
Neutrophil-to-lymphocyte ratio (NLR)	2.89 ± 1.39	2.85 ± 1.88	0.628
Platelet-to-Lymphocyte ratio (PLR)	121.91 ± 74.58	115.84 ± 39.06	0.799
Monocyte-to-Lymphocyte ratio (MLR)	0.27 ± 0.11	0.37 ± 0.16	**0.019**
Derived neutrophil-to-lymphocyte ratio	2.22 ± 1.02	1.88 ± 0.95	0.066



HC: Hypercholesterolemia; HT: Hypertension; DM: Diabetes mellitus; CAD: coronary artery disease; CRF: chronic renal failure; MI: myocardial infarction; Car.AD: carotid artery disease; P-AF: Prior atrial fibrillation; P-CABG: Prior coronary artery bypass graft

Figure 1. Preoperative variables of the patients

Monocyte/lenfocyte ratio (MLR) had increased significantly (Figure 2, 3). Arteriosclerosis is considered a chronic low-grade inflammatory disease. The degree of such an inflammatory process strongly correlates with the extent and severity of atherosclerotic disease.[14]

Preoperative serum concentration of CRP in patients undergoing coronary artery bypass surgery is an important determinant of postoperative stroke. In previous studies, increased serum CRP levels have shown poor outcome in patients with unstable angina, myocardial infarction and ischemic stroke.[6,15] This study showed that there is a significant relationship between perioperative serum concentration of CRP and the development of stroke after CABG.

According to previous studies, the ratio of monocytes to lymphocytes (MLR) has been reported as a novel indicator of inflammation. Thus, our study was the important to conduct more in-depth research on the relationship between MLR and the postoperative stroke. Previous studies have also shown that increased MLR was considered an independent risk factor in patients with ischemic stroke. At the same time, MLR has been associated with cardioembolic stroke, and carotid stenosis in ischemic stroke.[16] In our study, high MLR was associated with postoperative stroke. This suggests that we should pay attention to MLR in preoperative period.

The value of off-pump over conventional coronary artery bypass surgery in reducing the risk of postoperative stroke is controversial.[17] While concomitant valvular procedures increasing numbers of vessels grafted and on-pump CABG were not a significant predictor of stroke in this study; some studies have shown that off-pump CABG is being increasingly used for patients requiring coronary revascularization who are at high risk for the development of postoperative stroke as well as other complications resulting from CPB.[5,18,19]

There are several limitations to the present study. The first is the small number of patients. Second, some risk factors such as calcified arteriosclerotic aorta and duration of CPB were not considered. Despite these limitations, the study represents important results on postoperative stroke after CABG.

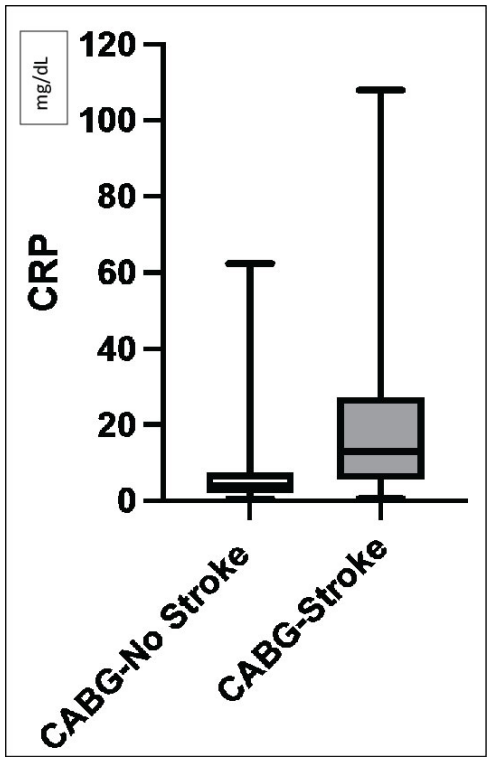


Figure 2. Distribution of preoperative serum concentration of C-reactive protein (CRP)

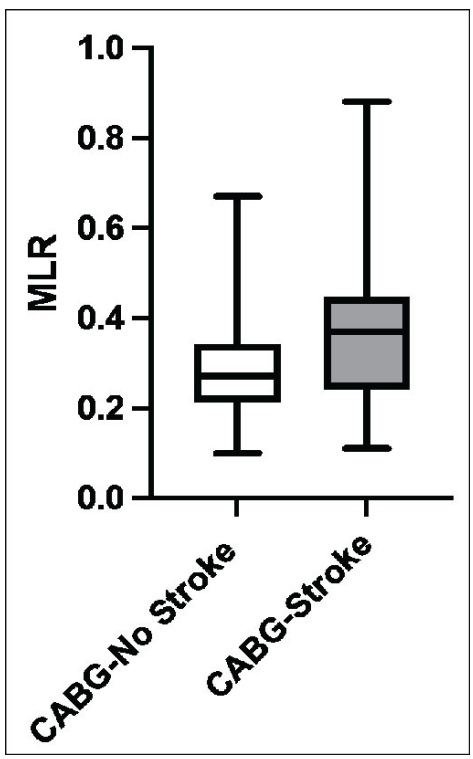


Figure 3. Ratio of monocytes to lymphocytes (MLR) in patients

In conclusion, Five variables (chronic renal failure, prior CABD, prior carotid artery disease, preoperative CRP levels and Monocyte/Lymphocyte ratio) were found to be associated with more perioperative stroke events. Postoperative stroke is a major contributor to mortality, prolonged hospitalization and other adverse postoperative complications. Identifying high risk patients who will develop stroke after CABG will reduce the risk of postoperative stroke.

DISCLOSURE

Ethics: The study was approved by the ethics committee of Lokman Hekim University (Decision number: 2023/35-13.03.2023).

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Conflict of interest: None

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