The effect of preoperative circadian blood pressure pattern on early postoperative outcomes in patients with coronary artery bypass graft surgery

Koroner arter baypas operasyonlu hastalarda preoperatif sirkadiyan kan basıncı paterninin erken postoperatif seyir üzerindeki etkisi

Muzaffer Bahçivan, Okan Gülel, Fersat Kolbakır*

From Departments of Cardiovascular Surgery and *Cardiology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey

Abstract

Objective: The aim of this prospective study was to evaluate the relationship between preoperative circadian blood pressure pattern and early postoperative course in patients undergoing coronary artery bypass graft (CABG) surgery.

Methods: One hundred and thirty patients planning to undergo isolated CABG operation were included to the study (80 men; 50 women). All patients were studied with ambulatory blood pressure monitoring performed 24 hours before surgery and were divided into 2 groups according with presence (79 patients) or absence (51 patients) of dipper phenomenon. Non-dippers were defined as those with a nocturnal reduction of systolic and diastolic blood pressures of less than 10% of daytime pressures. Both groups were compared with each other from the aspect of postoperative need for intraaortic balloon counterpulsation (IABP), inotropic drug support, extubation time, length of intensive care unit and hospitalization stays, renal failure, stroke, malignant ventricular arrhythmia, atrial fibrillation, postoperative myocardial infarction and cardiac mortality. Statistical analyses were performed using Chi-square, unpaired t and Mann-Whitney U tests. Logistic regression analysis was performed to establish associations of non-dipper phenomenon with the risk of postoperative complications.

Results: When compared with the dipper patients, need for inotropic medications (37.5% vs. 62.5%), low cardiac output syndrome (30.4% vs. 69.6%), postoperative myocardial infarction (28.6% vs. 71.4%) and malignant ventricular arrhythmias (27.8% vs. 72.2%) were higher in the non-dipper patients ($p<0.05$ for all). Logistic regression analysis demonstrated that non-dipper phenomenon after CABG was associated with longer cardiopulmonary bypass time (OR=1.038, 95%CI 1.016-1,060, p=0.001), more need for postoperative inotropic agent (OR=4.014, 95%CI 1.235-13,047, p=0.021) and postoperative IABP (OR=6.625, 95%CI 1.564-28.069, p=0.01) support, higher risk of low cardiac output syndrome (OR=4.159, 95%CI 0.921-18.775, p=0.064), malignant ventricular arrhythmia (OR=4.653, 95%CI 0.964-22,456, p=0.056) and postoperative myocardial infarction (OR=7.629, 95%CI 1.448-40.177, p=0.017).

Conclusion: Dipper and non-dipper phenomenon can be used as a simple analysis tool for assessing early postoperative mortality and morbidity. *(Anadolu Kardiyol Derg 2008; 8: 354-9)*

Key words: Dipper, non-dipper, ambulatory blood pressure monitoring, coronary artery bypass surgery, hypertension, morbidity, logistic regression analysis

Özet

Amaç: Bu prospektif çalışmanın amacı koroner arter baypas greftleme (KABG) operasyonu olan hastalarda, preoperatif sirkadiyan kan basıncı paterninin erken postoperatif seyir üzerindeki etkisini araştırmaktır.

Yöntemler: İzole KABG operasyonu planlanan 130 hasta (80 erkek, 50 kadın) çalışmaya dâhil edildi. Bütün hastalarda operasyondan 24 saat önce kan basıncı ölçümleri yapıldı ve hastalar dipper (79 hasta) ve non-dipper (51 hasta) fenomenin varlığına göre 2 gruba ayrıldı. Gecelik sistolik ve diyastolik kan basıncı değerleri %10'dan daha az düşen hasta grubu non-dipper olarak tanımlandı. Her iki grup postoperatif intraaortik balon pompası (IABP) ihtiyacı, inotrop ilaç ihtiyacı, ekstübasyon zamanı, yoğun bakımda ve hastanede kalış süresi, renal yetersizlik, inme, malign ventriküler aritmi, atriyal fibrilasyon, düşük kardiyak debi sendromu, postoperatif miyokard infarktüsü ve mortalite açısından karşılaştırıldı. İstatistiksel değerlendirmede Ki-kare, eşleştirilmemiş t ve Mann Whitney U testleri kullanıldı. Non-dipper fenomeni ile postoperatif komplikasyon riskleri lojistik regresyon analizi yapılarak araştırıldı.

Address for Correspondence/Yazışma Adresi: Dr. Muzaffer Bahçivan, Department of Cardiovascular Surgery, Faculty of Medicine Ondokuz Mayıs University 55139 Kurupelit, Samsun, Turkey Phone: (office): +90 362 3121919 (extension 3110) Mobile: +90 533 226 10 92 Fax: +90 362 457 60 41 E-mail: fatos.mbahcivan33@yahoo.com

Bulgular: Dipper karakter gösteren hastalarla karşılaştırıldığında, non-dipper grupta inotropik ilaç ihtiyacı (%37.5'a %62.5), düşük kardiyak debi sendromu (%30.4'a %69.6), postoperatif miyokard infarktüsü (%28.6'e %71.4) ve malign ventriküler aritmiler (%27.8'e %72.2) daha fazlaydı (p<0.05). Lojistik regresyon analizinde sonuçlar şu şekildeydi; kardiyopulmoner baypas zamanı (OR=1.038, %95GA 1.016-1.060 p=0.001), postoperatif inotropik ajan ihtiyacı (OR=4.014, %95GA 1.235-13.047, p=0.021), düşük kardiyak debi sendromu (OR=4.159, %95GA 0.921-18.775, p=0.064), malign ventriküler aritmi (OR=4.653, %95GA 0.964-22.456, p=0.056) postoperatif IABP ihtiyacı (OR=6.625, p=0.010, %95GA(1.564-28.069), postoperatif miyokard infarktüsü (OR=7.629, %95GA 1.448-40.177, p=0.017).

Sonuç: Dipper ve non-dipper fenomen, KABG operasyonu geçirecek hastalarda erken postoperatif mortalite ve morbiditeyi tayin etmede basit bir analiz yöntemi olabilir. *(Anadolu Kardiyol Derg 2008; 8: 354-9)*

Anahtar kelimeler: Dipper, non-dipper, ambulatuvar kan basıncı monitarizasyonu, koroner arter baypas cerrahisi, hipertansiyon, morbidite, lojistik regresyon analizi

Introduction

There are many risk factors for patients who will undergo coronary artery bypass graft (CABG) surgery. Many factors like left ventricular dysfunction, female gender, surgery at emergency conditions, obesity, renal failure, diabetes, peripheral or carotid artery disease may increase the risk for surgery (1). In addition to these risk indicators, determination of some subclinical conditions may help identification of patients at high risk and point out different monitoring needs.

Monitoring blood pressure for 24 hours provides valuable information about diurnal rhythm of blood pressure. Normally blood pressure levels decrease 10-20% during sleep and increase rapidly early in the morning. Decreases during sleep more than 20% are designated as extreme dipper state, decreases between 10-20% are designated as dipper state and decreases less than 10% are designated as non-dipper state (2, 3). By using 10% diurnal–nocturnal difference as a cut-off point to define non-dippers, Staessen et al. found (4) a 22% prevalence of non-dippers among men and a 21% prevalence among women.

Previous studies revealed that cerebrovascular accident, chronic heart disease and renal disease due to end organ damage were more frequent in patients who were in non-dipper group (5-9). Moreover, it was reported that being a non-dipper was an independent risk factor for cardiovascular diseases (10-15). In hemodialysis patients, mean left ventricular mass index was significantly higher in the non-dipper group (16).

It was shown that changes in circadian rhythm profile were determining development of cardiovascular events, however, information about the effects of those changes in patients undergoing CABG operations and relation of preoperative circadian blood pressure changes with postoperative course is not known exactly. In the study of Ceyhan et al. (17), only circadian rhythm characteristics of blood pressure and heart rate of patients before and after CABG surgery were evaluated.

In our study, we aimed to investigate the relationship between preoperative circadian blood pressure pattern and early postoperative course in patients with CABG surgery.

Methods

One hundred and thirty patients (80 males, 50 females) waiting for isolated CABG surgery at the Cardiovascular Surgery Department of Ondokuz Mayıs University Medical Faculty were included in this prospective study between January 2004 and June 2005. All medications of the patients were stopped two days before hospitalization. Patients exposing to risk in the case of medication withdrawal were not enrolled to the study. The study was conducted in accordance with the recommendations found in the Helsinki Declaration. Informed consent was taken from all participants. Their physical examinations were performed and electrocardiograms, echocardiograms and routine laboratory tests were obtained. Patients with coexisting neurological disease, recent myocardial infarction, cardiac arrhythmia and low ejection fraction (<40%) were excluded in order to eliminate their effects on postoperative outcomes. Additionally, hypertensive patients were not recruited for the correct interpretation of preoperative 24-hour ambulatory blood pressure monitoring.

All patients underwent conventional CABG operation. Twenty-three patients had single, 28 patients had double, and 79 patients had three or more vessels bypass surgery. After the operation, need for intraaortic balloon counterpulsation (IABP) or inotropic drug support, occurrence of low cardiac output syndrome (LCOS), malignant ventricular arrhythmias or atrial fibrillation, development of postoperative myocardial infarction, extubation time, length of intensive care unit (ICU) stay, neurological or renal complications, discharge time and cardiac mortality were recorded.

Patients requiring inotropic medications more than 12 hours postoperatively were accepted as inotropic dependent. Adrenaline, dopamine or dobutamine were used alone or in combination as an inotropic agent. Ventricular tachycardia and ventricular fibrillation were defined as malignant arrhythmias. Amiodarone, lidocaine or electrical cardioversion were used for their treatment. Beta-blocker, verapamil, diltiazem or amiodarone were used for treatment of atrial fibrillation. Diagnosis of myocardial infarction was established by electrocardiography and elevated troponin I levels.

Ambulatory blood pressure monitoring

24-hour blood pressure monitoring recordings of all patients were obtained before the operation day. Ambulatory Blood Pressure Monitoring Spacelabs 90207 instrument (Space Labs Inc, Richmond, Washington, USA) was used for this purpose. Blood pressure measurements were obtained with 15-minute intervals during daytime and with 20-minute intervals during sleep. Daytime and night periods were defined based on patient diary. Systolic and diastolic blood pressure measurements during daytimes and nights were evaluated. Decrease in mean systolic and diastolic blood pressure levels less than 10% during nights versus daytimes was defined as a

non-dipper state. The decrease over this threshold was defined as a dipper state. Extreme dippers with blood pressure decrease of more than 20% were included to the dippers.

CABG surgery

All operations were performed between 08:00-13:00 hours during the day. Thiopental sodium (1-3 mg/kg) and phentanil (3-5 µg/kg) were used for induction of anesthesia. Volatile agents were administered with a mixture of 50% air and O_2 for the maintenance. Propofol infusion was administered at the dose of 3 mg/kg/hour during cardiopulmonary bypass. Neuromuscular blockage was provided via pancuronium bromide (0.1-0.15 mg/kg). Alpha-Stat acid-base protocol was used for arterial blood gas analysis. Following standard median sternotomy, left internal mammary artery grafts were prepared. Cardiopulmonary bypass was performed by standard aortic two stage venous cannulation. Systemic hypothermia at 28°C was applied to all patients. Cold blood cardioplegia with antegrade intervals and cold topical irrigation with +4°C ringer lactate were used for myocardial protection. Cold blood cardioplegia was prepared. Cardioplegia solution was made hyperkalemic by addition of potassium at the dose of 20 mEq/L during induction and 10 mEq/L during maintenance. Antegrade cardioplegia with hyperkalemic cold blood administration from aorta root was induced with a dose of 10 ml/kg at the beginning of ischemia and of 5 ml/kg at the maintenance with intervals of 20 minutes. While distal anastomoses were performed with a single cross-clamp period at arrested heart, proximal anastomoses were made with partial clamps at beating heart. Analyses for electrolyte levels (Na, K, Cl, Ca) and blood gases (pH, pCO2, pO2, HCO3) were performed routinely during and after cardiopulmonary bypass surgery. Electrolyte imbalance or acidosis was corrected before removal of cross-clamp.

Statistical analysis

Statistical analyses were performed with SPSS for Windows, version 10.0 (SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution. Unpaired Student's t-test was applied for comparison of continuous data showing normal distribution and Mann-Whitney U test was applied for comparison of data showing abnormal distribution. Categorical variables were analyzed with Chi-square test. Continuous variables were expressed as a mean and non-continuous variables were expressed as a ratio. Logistic regression analysis was performed to establish associations of non-dipper phenomenon with the risk of postoperative complications. The dependent variable was presence or absence of dipper phenomena, and independent variables were age, cardiopulmonary bypass time, postoperative inotropic agent need, low cardiac output syndrome, malignant ventricular arrhythmia, postoperative IABP need, postoperative myocardial infarction, gender, and smoking. The level for statistical significance was accepted as $p<0.05$.

Results

Seventy-nine participants were in dipper state and 51 participants were in non-dipper state. Twenty-two patients were in extreme dipper state and were included to the dipper group. Mean 24-hour blood pressure measurements and heart rates of patients are presented in Figure 1. There were no any significant differences between dippers and non-dippers according to basal clinical characteristics, left ventricular ejection fraction and Euroscores ($p>0.05$ for all) (Table 1).

Intraoperative and postoperative data are presented in Table 2.

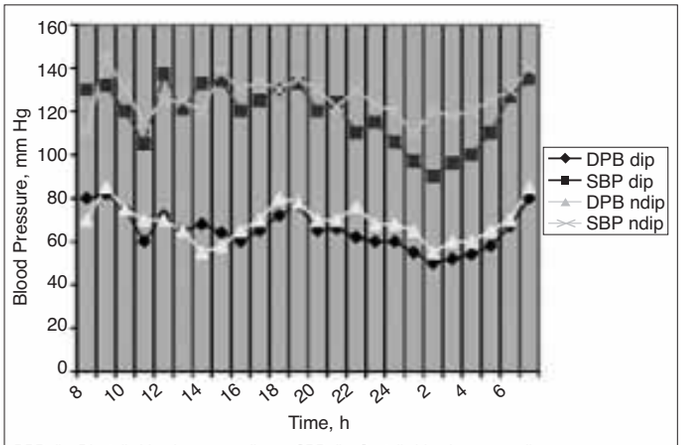
The incidences of need for inotropic medications (62.5% vs. 37.5%, p=0.001), LCOS (69.6% vs. 30.4%, p=0.002), postoperative myocardial infarction (71.4% vs. 28.6% p=0.02) and malignant ventricular arrhythmias (72.2% vs. 27.8%, p=0.005) were higher in non-dipper patients than in dipper patients ($p<0.05$ for all).

Myocardial infarction occurred in four patients of dipper group and in nine patients of non-dipper group at postoperative period and appropriate treatment was applied to those patients. As a neurological complication, hemiplegia occurred in one patient of dipper group and in two patients of non-dipper group. Hemiplegia became persistent in that patient of dipper group. One of the patients who developed renal failure postoperatively in the non-dipper group required dialysis. Seven patients died at early postoperative period. Four of them were in the dipper group and causes of death were as follows: hemorrhage (n=2), early LCOS (n=2). Three deaths were in the

Table1. Comparison of baseline characteristics of dipper and non-dipper patients

Parameters	Dipper group (n=79)	Non-dipper group (n=51)	*p
Mean age, years	63.56±11.92 66 (38-82)	66±10.96 68.50 (39-82)	0.295
Male/female, n	46/33	34/17	0.435
Smoking, n (%)	24 (68.6)	11 (31.4)	0.366
Obesity, n (%)	24 (63.2)	14 (36.8)	0.872
Ejection fraction, %	48.28±8.6 48 (30-65)	49.50 (28-65) 48.52±9.92	0.758
Euroscore	329.90±168.56 325 (88-614)	332.26±190.53 273 (122-887)	0.862

Data are represented as Mean±SD, Median (Max-Min) values and proportion/percentage
*- Chi-square test for comparison of categorical variables, unpaired t test and Mann Whitney U test for comparison of continuous variables



DBP dip: Diastolic blood pressure dipper; SBP dip: Systolic blood pressure dipper
DBP ndip: Diastolic blood pressure non dipper; SBP ndip: Systolic blood pressure non dipper

Figure 1. 24-hour blood pressure measurements showing dipper and non-dipper status

non-dipper group and their causes were renal failure (n=1), sepsis due to pulmonary failure (n=1) and early LCOS (n=1).

Logistic regression analysis (Table 3) demonstrated that the risk of postoperative myocardial infarction development was 7 times (OR=7.629, 95%CI 1.448-40.177, p=0.017), IABP need - 6.6 times (OR=6.625, 95%CI 1.564-28.069, p=0.01), postoperative inotropic agent need (OR=4.014, 95%CI 1.235-13,047, p=0.021), low cardiac output syndrome (OR=4.159,95%CI 0.921-18.775, p=0.064) and malignant ventricular arrhythmia (OR=4.653, 95%CI 0.964-22,456, p=0.056) were 4 times greater in nondipper phenomenon patients than in the patients with dipper phenomenon after CABG.

Discussion

Our study describes the effects of circadian rhythm characteristics on operative outcomes in patients with CABG surgery. We evaluated whether or not preoperative non-dipper pattern affects postoperative course and demonstrated that non-dipper pattern before CABG surgery was related with higher incidence of postoperative need for positive inotropic agents, arrhythmias and LCOS than dipper pattern.

Many cardiovascular events show circadian periodicity. Their peak incidences are during the first hours following awakening. Ischemic cardiac events mostly occur between 6-10 A.M. (9, 10). Some other events like cerebrovascular accident, transient ischemic attack or stroke are more frequent also during these hours (5, 7). It is suggested that concentrations of circulating catecholamines, renin and cortisol increase early in the morning and induce vascular tonus (10). Consequently, vasoconstriction of coronary arteries may lead to myocardial ischemia. Moreover, increased catecholamine levels may induce life-threatening arrhythmias. In addition, changes in thrombocyte activity and fibrinolytic system during early hours of the day may lead to thromboses (15, 17-21). Ceyhan and colleagues (17) measured preoperative blood pressures for 24 hours in patients underwent CABG surgery and found that 73% of their patients were non-dippers. They concluded that relatively higher incidence of non-dipper character in candidates for CABG surgery might be due to autonomic nervous system dysfunction related with coronary artery disease (17).

Non-dippers may have a worse cardiovascular prognosis, both for stroke and for cardiac events. Increased blood pressure and left ventricular stroke volume lead to fissures in coronary plaques and increase vascular tonus in non-dipper patients even if they are normotensives. With the decrease in coronary blood flow, thrombocyte aggregation increases and fibrinolytic activity decreases. All of these mechanisms lead to arterial thrombosis and result in acute myocardial infarction or sudden cardiac death (18-21). Also, supraventricular and ventricular arrhythmias have been found to be more prevalent

Table 2. Comparison of intraoperative and postoperative characteristics of dipper and non-dipper patients

Variables	Dipper group (n=79)	Non-dipper group (n=51)	*p
Distal anastomosis, number	3.00±1.01 3 (1-6)	2.88±1.01 3 (1-5)	0.359
CPB time, min	108.00±32.68 105 (45-180)	96.76±21.82 91.5 (40-145)	0.032
Cross-clamp time, min	67.06±22.97 67 (20-124)	65.02±20.65 64.50 (20-103)	0.607
Discharge time, days	6.72±1.17 7 (5-9)	7.0±1.2 7 (5-9)	0.183
Extubation time, hours	9.16±5.12 8 (2-24)	9.24±5.40 8 (2-24)	0.994
ICU stay time, hours	27.09±18.43 22 (10-96)	27.40±20.29 22 (10-106)	0.944
Postoperative inotropic agent need, n(%)	15 (37.5)	25 (62.5)	0.001
Low cardiac output syndrome, n(%)	7 (30.4)	16 (69.6)	0.002
Malignant ventricular arrhythmia, n(%)	5 (27.8)	13 (72.2)	0.005
Atrial fibrillation, n(%)	18 (52.9)	16 (47.1)	0.377
Postoperative mortality, n(%)	4 (40)	6 (60)	0.189
Postoperative IABP need, n(%)	4 (33.3)	8 (66.7)	0.061
Postoperative myocardial infarction, n(%)	4 (28.6)	10 (71.4)	0.020
Renal failure, n(%)	2 (66.7)	1 (33.3)	1.00
Stroke, n(%)	3 (75)	1 (25)	1.00

Data are represented as Mean±SD, Median (Max-Min) values and number/percentage
* - Chi-square test for comparison of categorical variables, unpaired t test and Mann Whitney U test for comparison of continuous variables
CPB - cardiopulmonary bypass, IABP-intraaortic balloon counterpulsation, ICU - intensive care unit

Table 3. Logistic regression analysis data

Variables	OR	95 % CI		p
		Lower	Upper	
Age	0.994	0.952	1.039	0.799
Cardiopulmonary bypass time	1.038	1.016	1.060	0.001
Postoperative inotropic agent need	4.014	1.235	13.047	0.021
Low cardiac output syndrome	4.159	0.921	18.775	0.064
Malignant ventricular arrhythmia	4.653	0.964	22.456	0.056
Postoperative IABP need	6.625	1.564	28.069	0.010
Postoperative myocardial infarction	7.629	1.448	40.177	0.017
Gender	1.436	0.536	3.848	0.472
Smoking	0.341	0.103	1.131	0.079

CI - confidence interval, CPB - cardiopulmonary bypass, IABP-intraaortic balloon counterpulsation, OR - odds ratio

among non-dippers than dippers (22). The association of left ventricular hypertrophy and vagal deactivation may lead to prolongation of corrected Q-T interval potentially facilitating ventricular arrhythmias in non-dipper hypertensive patients (23). Non-dipping blood pressure profile may also be associated with endocrine conditions (i.e., hyperthyroidism, hyperparathyroidism, hyperaldosteronism, pheochromocytoma, hypercortisolism), renal dysfunction, ethnicity, disturbances in circadian plasma melatonin changes, and pre-eclamptic toxemia (3). In our study, one possible explanation of increased arrhythmias and LCOS, and increased need for inotropic medications and IABP in the non-dipper group may be the higher incidence of postoperative myocardial infarction in that group.

Many preoperative risk factors may affect postoperative course of patients who underwent CABG procedure. For this reason, our preoperative patient selection criteria were designed to minimize the impact of any coexisting factor on the outcome of CABG surgery. Patients with ejection fraction less than 40% were considered to be of high-risk for CABG surgery by our clinical protocol. Thus, patients with low ejection fraction were excluded from study. Patients with previous neurological disorder were also excluded since postoperative recovery of these patients may be more difficult or longer, potentially affecting the outcome data. In order to eliminate the preoperative impact of high blood pressure, we excluded patients with preoperative hypertension.

Limitations of the study

The clinical classification of some patients according to ambulatory blood pressure measurements may be affected from arm position or restricted activity at the hospital. The number of patients in both groups was relatively low.

Conclusion

Postoperative morbidity of patients showing non-dipper pattern before CABG surgery is higher. It may be suggested that non-dipper pattern is a risk factor for patients who will undergo CABG surgery and it should be taken into consideration at surgical planning. We emphasize that dipper/non-dipper phenomenon may be used for risk analysis as an easy and non-invasive method during early postoperative period in patients who will undergo CABG surgery. Further specific studies, either clinical or experimental, are mandatory to determine the effect of circadian rhythm of blood pressure on postoperative course in patients who will have CABG operations and have non-dipper status.

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Dr. Gülseren Engin