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Original Article

Investigation of the Effect of Asthma on Mortality and Morbidity After Coronary Artery Bypass Surgery

Sami İlhan[1], Sevil Özkan[2], Murat Başpınar[3], Cevdet Uğur Koçoğulları[3]

[1]Department of Respiratory Medicine, Dr Siyami Ersek Thoracic and Cardiovascular Surgery Research and Training Hospital, İstanbul, Turkey
[2]Department of Respiratory Medicine, Haydarpaşa Numune Research and Training Hospital, İstanbul, Turkey
[3]Department of Cardiovascular Surgery, Dr Siyami Ersek Thoracic and Cardiovascular Surgery Research and Training Hospital, İstanbul, Turkey

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Abstract

OBJECTIVES: No studies have been specifically conducted on asthma patients undergoing cardiac surgery for assessing mortality and morbidity. Distinct effects of cardiac surgery lead to negative effects on respiratory functions, putting patients with existing lung diseases under an increased risk. We aimed to investigate whether asthma patients are under higher risk for mortality and possible complications after coronary artery bypass graft (CABG) surgery than patients without asthma.

MATERIALS AND METHODS: The study included patients who underwent elective CABG surgery at our hospital between November 2014 and November 2015. Patients with a history of asthma were verified with physical examination and spirometric measurements by a single. The asthma group was compared with the controls in terms of mortality and morbidities.

RESULTS: Asthma patients were extubated later than control patients (p=0.028); however, prolonged intubation (longer than 24 h) frequency was not different (p>0.05). Asthma patients required longer stay in the intensive care unit (ICU) (p=0.003) than controls. The incidence of perioperative asthma exacerbations was significantly lower in patients in whom asthma was previously well-controlled. The incidence of postoperative sibilant rhonchi was lower in patients in whom asthma was under control than in those in whom asthma was partially controlled (p=0.020).

CONCLUSION: Asthma is associated with longer ICU stay and asthma-related pulmonary complications after CABG surgery. Preoperative evaluation of asthma patients scheduled for CABG surgery requires consideration of the control status of asthma. Studies with more controls are needed to provide further evidence on the topic.

KEYWORDS: Asthma, cardiac surgery, coronary artery bypass surgery

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INTRODUCTION

Asthma is a common disease characterized by hyperresponsiveness and reversible obstruction of the airways due to chronic inflammation [1, 2]. Perioperative pulmonary and extrapulmonary complications are increased in asthma patients undergoing surgery under sedation [3, 4]. Despite the low incidence of perioperative bronchospasm and laryngospasm, patients of advanced age and with uncontrolled asthma experience more complications than younger asthma patients or asthma patients with controlled symptoms [5]. Histories of asthma-related emergency department visits, hospitalizations, stay in the intensive care unit (ICU), and use of systemic corticosteroids are independent contributing factors for postoperative complications in asthma patients [6], with an emergency visit within 3 months preoperatively doubling the risk of postoperative mortality and asthma hospitalization tripling the risk of postoperative pneumonia [6].

Cardiopulmonary bypass causes neutrophil recruitment in the pulmonary microvascular bed, formation of free oxygen radicals, impaired alveolar stability by changing the structure of the alveolar surfactant, and triggered complement cascade. This distinct effect leads to negative effects on respiratory functions following cardiac surgery [7], putting patients with existing lung diseases under increased risk.

No studies have been specifically conducted on asthma patients undergoing cardiac surgery to assess mortality and morbidity. This study aimed to investigate whether asthma patients are under greater risk for mortality, pulmonary and nonpulmonary complications, longer ICU stay, and other morbidities after coronary artery bypass graft (CABG) surgery than patients without asthma.

Address for Correspondence: Murat Bastopcu, Department of Cardiovascular Surgery, Dr Siyami Ersek Thoracic and Cardiovascular Surgery Research and Training Hospital, İstanbul, Turkey
E-mail: muratbastop@gmail.com

MATERIALS AND METHODS

Patients

The study retrospectively included patients who underwent elective CABG surgery at our hospital's Cardiovascular Surgery Clinic between November 2014 and November 2015. Patients with missing records, chronic obstructive pulmonary disease and/or bronchiectasis, and concomitant valvular heart disease and patients undergoing additional operations to CABG surgery were excluded. Patients with a history of asthma were verified for their diagnosis with a physical examination and spirometric measurements by a single pulmonologist. Approval from the institutional ethics board was obtained (2801928-604-02) and due to the retrospective design of the study individual patient consents were waived. The study was carried out in accordance with the Helsinki Declaration.

Asthma patients were assessed for asthma control levels as described in the Global Initiative for Asthma (GINA) Guidelines [8]. The Asthma Control Test (ACT) is a 5-item questionnaire on asthma symptoms during the day and night, the use of rescue medication, and the level of exposure to daily activities owing to asthma [9, 10]. The ACT was performed 1 day before surgery. Patients with controlled and uncontrolled asthma were further analyzed for mortality and morbidity. When ACT scores were grouped, patients who received ≥20 points were considered to have "controlled" asthma and those who received <20 points were considered to have "uncontrolled" asthma [8].

Definitions

Pulmonary function tests were routinely performed using a computerized adaptive spirometer (ZAN 100 spirometer, nSpire Health, Longmont, CO, United States) approximately 1 week before surgery and with patients in the sitting position. The best out of three consecutive tests was approved for analysis. The measured forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) values were recorded in liters. Expected values were taken from the device's data for the expected value for the Caucasian race.

Asthma attack was defined clinically as an exacerbation of known asthma with worsened symptoms of wheezing and dyspnea, together with sibilant rhonchi on a physical examination. Any asthma attack following extubation in the ICU until discharge from the hospital was recorded. Prolonged intubation was defined as intubation exceeding 24 h, prolonged ICU stay as hospitalization in the ICU for more than 24 h, and prolonged hospitalization as hospitalization for more than 7 days. Postoperative bradyarrhythmia or tachyarrhythmia was recorded as arrhythmia. New and progressive infiltrations on the chest radiograph and the presence of at least two of the following criteria were necessary for the diagnosis of pneumonia: fever (>38°C), purulent tracheobronchial secretions, and leukocytosis (>10,000/mm^3). Renal impairment was defined as a postoperative increase in creatinine by >0.7 mg/dL from baseline value or above to above 1.8 mg/dL, per criteria for renal damage, or the requirement for hemodialysis; cerebrovascular events were defined as regional neurological dysfunction for more than 24 h; and mortality was defined as death due to any cause before discharge from the hospital. Both groups were compared in terms of mortality and morbidity, frequency of asthma attacks, rate of respiratory distress, and presence of postoperative rhonchus. The effect of the asthma control score on mortality and morbidity was further investigated in the asthma group.

MAIN POINTS

- Asthma patients are not under increased risk for mortality after coronary artery bypass grafting surgery.
- Preoperative asthma control is important for prevention of asthma exacerbations in the postoperative period of coronary artery bypass grafting surgery.
- Asthma patients should be reviewed for their symptoms and asthma control status whenever possible before undergoing cardiac operations.

Operative Method

Following median sternotomy and heparinization, moderate (28°C) systemic hypothermia was achieved with arterial cannulation of the ascending aorta and venous cannulation of the right atrium. Myocardial protection was performed with intermittent isothermic blood cardioplegia. The left internal mammary artery and saphenous vein were used as bypass grafts. Proximal anastomoses were performed on the aorta with a lateral clamp. Mechanical and pharmacological support was applied to wean from cardiopulmonary bypass at the end of the operation when necessary.

Statistical Analysis

Number Cruncher Statistical System 2007 (Kaysville, UT, USA) was used for statistical analysis. The Shapiro-Wilk test and box plot graphs were used to test for normality. Variables with normal distribution are shown in the tables with their mean and standard deviations, and Student's t test was used to compare groups for these variables with normal distribution. Variables without normal distribution are shown as minimum-maximum and median values, and the Mann-Whitney U test was performed to compare groups. Qualitative data were compared using cross-tabulation analysis. For 2x2 tables, the Pearson chi-square test was applied, except when expected counts in groups were lower than 5 where Fisher's exact test and Yates' continuity correction (chi-square with Yates correction) were applied. For 2x3 tables, the Fisher-Freeman-Halton Exact test was applied for correction. The significance threshold was set at $p<0.05$.

RESULTS

Evaluation of Demographic Characteristics and Spirometry Data

The study was conducted with 52 asthma patients and 53 consecutive nonasthmatic controls who underwent isolated CABG surgery. The demographic data of patients in the asthma and control groups are given in Table 1. In our study, diabetes and hypertension were the most common comorbid diseases in patients in the asthma and control groups who had undergone CABG surgery, and no statistically significant

Table 1. Evaluation of demographic and spirometry data by group

		Total (n=105)	Asthma (n=52)	Control (n=53)	p
Gender	Female	44 (41.9)	31 (59.6)	13 (24.5)	[a]0.001*
Age (years)	Mean±SD	61.63±9.65	63.04±10.52	60.25±8.59	[b]0.139
BMI (kg/m^2)	Mean±SD	29.90±4.68	29.84±5.19	29.96±4.17	[b]0.898
Family history of asthma	No	68 (64.8)	15 (28.8)	53 (100.0)	[a]0.001*
Smoking	Ever smoker	72	34 (15.4%)	38 (64.2%)	[a]0.327
	Never smoker	33	19 (84.6%)	14	
Creatinine	Min-Max (Median)	0.43-8.35 (0.9)	0.56-7.8 (0.9)	0.43-8.35 (0.9)	[c]0.414
Diabetes	Yes	56 (53.3)	29 (55.8)	27 (50.9)	[a]0.764
Hypertension	Yes	53 (50.5)	30 (57.7)	23 (43.4)	[a]0.204
Multivessel disease	n (%)	100 (95.2%)	50 (96.2%)	50 (94.3%)	[a]0.663
Euroscore	Mean±SD	3.5±2.2	3.1±2.2	3.8±1.9	[b]0.305
Ejection fraction	Mean±SD	55.5±7.6	54.2±8.4	56.7±6.1	[b]0.163
FVC (%)	Mean±SD	88.23±17.57	79.36±16.29	96.93±14.19	[b]0.001*
FEV_1 (%)	Mean±SD	90.62±20.53	78.11±18.26	102.9±14.35	[b]0.001*
FEV_1/FVC	Mean±SD	84.54±7.8	83.09±9.46	85.97±5.45	[b]0.001*

[a]Yates' Continuity Correction; [b]Student's t-test; [c]Mann-Whitney U test; *p<0.05; BMI: Body Mass Index; FVC: Forced Vital Capacity; FEV_1: Forced Expiratory Volume in 1 second

Table 2. Evaluation of demographic and spirometry data by group

		Total (n=105)	Asthma (n=52)	Control (n=53)	p
Operation time (min)	Mean±SD	98.99±24.96	103.1±29.27	94.96±19.29	[a]0.130
Cross-clamp time (min)	Mean±SD	66.02±19.05	68.06±21.21	64.02±16.63	[a]0.230
Time to extubation (h)	Mean±SD	12.68±22.77	14.23±32.03	11.15±5.05	[a]0.028*
ICU stay (days)	Mean±SD	1.57±1.57	2.04±2.1	1.11±0.42	[a]0.003*
Prolonged intubation	n (%)	7 (6.7)	3 (5.8)	4 (7.5)	[b]1.000
Prolonged intensive care stay	n (%)	20 (19.0)	15 (28.8)	5 (9.4)	[b]0.022*

[a]Student's t-test; [b]Fisher's exact test; *p<0.05; ICU: Intensive Care Unit

differences were determined between the two groups in terms of these comorbidities.

Spirometry values in the asthma and control groups are included in Table 1. FVC (%), FEV_1 (%), and FEV_1/FVC in the asthma group were found to be significantly lower than those in the control group (p<0.01).

Evaluation of Perioperative and Intensive Care Data

Perioperative data are given in Table 2. Operation and cross-clamp times were similar in the two groups. Asthma patients were on average extubated later than control group patients (14.23±32.03 vs 11.15±5.05 h, p=0.028), but prolonged extubation (longer than 24 h) was not a feature of asthma patients (p>0.05). Longer stay in the ICU (2.04±2.01 vs 1.11±0.42 days, p=0.003), with more patients with prolonged ICU stay, however, was more prominent in asthma patients than control group patients.

Evaluation of Mortality and Postoperative Complications

Postoperative mortality and morbidity in the groups are given in Table 3. When groups were compared in terms of mortality, no significant difference was observed. The rate of prolonged hospitalization in the asthma group was higher than that in the control group, albeit it was not statistically significant (p=0.064). All detected cases of pneumonia were in the asthma group, but the sample size was small to deduce significance. No difference was detected concerning other morbidities.

Postoperative data on asthma control scores are given in Table 4. Of the 52 asthma patients, 61.5% had controlled asthma while 38.5% had uncontrolled asthma. A statistically significant difference was detected in the rate of asthma attacks with respect to asthma control (p=0.048). The rate of asthma attacks was significantly lower in patients in whom asthma was under control: 75% in the uncontrolled group and 44% in the controlled group.

The difference in the rates of postoperative sibilant rhonchi with respect to asthma control was also significant (p=0.034). With paired comparison, the incidence of postoperative sibilant rhonchi in patients in whom asthma was under control was lower than that in whom it was uncontrolled (p=0.020).

Table 3. Comparison of mortality and morbidity in the asthma and control groups

	Total (n=105) n (%)	Asthma (n=52) n (%)	Control (n=53) n (%)	p
Gastrointestinal bleeding	2 (1.9)	2 (3.8)	-	[a]0.243
Acute renal failure	2 (1.9)	2 (3.8)	-	[a]0.243
Arrhythmia	31 (29.5)	18 (34.6)	13 (24.5)	[a]0.358
Prolonged hospitalization	29 (27.6)	18 (34.6)	11 (20.8)	[b]0.064
Reintubation	3 (2.9)	1 (1.9)	2 (3.8)	[a]1.000
Hypotensive shock	4 (3.8)	3 (5.8)	1 (1.9)	[a]0.363
Intrathoracic hemorrhage	9 (8.6)	5 (9.6)	4 (7.5)	[a]0.741
Cerebrovascular event	1 (1.0)	-	1 (1.9)	[a]1.000
Tamponade	1 (1.0)	-	1 (1.9)	[a]1.000
Reoperation for bleeding	7 (6.7)	3 (5.8)	4 (7.5)	[a]1.000
Pulmonary edema	7 (6.7)	1 (1.9)	6 (11.3)	[a]0.113
Pneumonia	4 (3.8)	4 (7.7)	-	[a]0.057
Pleural effusion	32 (30.5)	18 (34.6)	14 (26.4)	[c]0.402
Phrenic nerve palsy	1 (1.0)	1 (1.9)	-	[a]0.495
Pneumothorax	1 (1.0)	1 (1.9)	-	[a]0.495
Mortality	4 (3.8)	2 (3.8)	2 (3.8)	[a]1.000

[a]Fisher's exact test; [b]Fisher-Freeman-Halton test; [c]Yates' Continuity Correction

Table 4. Effect of asthma on mortality and morbidity in patients with controlled and uncontrolled asthma

	Asthma control level		
n=52	Controlled 32 (61.5%) n (%)	Uncontrolled 20 (38.5%) n (%)	p
Gastrointestinal bleeding	-	2 (10.0)	0.068
Acute renal failure	1 (3.1)	1 (5.0)	0.732
Arrhythmia	9 (28.1)	9 (45.0)	0.213
Reintubation	-	1 (5.0)	0.202
Hypotensive shock	1 (3.1)	2 (10.0)	0.301
Intrathoracic hemorrhage	3 (9.4)	2 (10.08)	0.941
Reoperation for bleeding	2 (6.3)	1 (5.0)	0.851
Pulmonary edema	1 (3.1)	-	0.425
Pneumonia	3 (9.4)	1 (5.0)	0.565
Pleural effusion	11 (34.4)	7 (35.0)	0.963
Phrenic nerve palsy	-	1 (5.0)	0.202
Pneumothorax	1 (3.1)	-	0.425
Readmission within 30 days	1 (3.1)	-	0.425
Prolonged hospitalization	11 (34.4)	7 (35.0)	0.923
Mortality	1 (3.1)	1 (5.0)	0.732
Asthma attack	14 (43.8)	15 (75.0)	0.027*
Postoperative sibilant rhonchi	20 (62.5)	19 (95.0)	0.008*

Fisher's exact test; *p<0.05

DISCUSSION

Our results show that asthma does not appear to affect mortality after cardiac surgery. No difference in mortality was seen in asthma and control patients or in uncontrolled and controlled asthma patients. In terms of morbidity, the only significant adverse outcome was found to be longer ICU stay and the presence of sibilant rhonchi after surgery, especially with uncontrolled asthma. Therefore, we could not deduce that asthma has an effect on mortality or morbidity other than possible exacerbation of asthma symptoms after cardiac surgery.

The deleterious effects of cardiopulmonary bypass, with neutrophil recruitment in the pulmonary microvascular bed, formation of free oxygen radicals, changes in the structure of the alveolar surfactant, and triggered complement cascade, lead to negative effects on respiratory function [7], creating a hazardous setting for asthma patients in the perioperative period.

Recent studies on noncardiac surgery have shown that asthma patients in the stable phase do not carry a higher risk of postoperative respiratory complications than other patients [5]. In a retrospective study conducted in noncardiac surgery patients by Warner et al. [11], no deaths were reported among 706 asthma patients, while 1.7%, 0.1%, and 0.3% of patients developed bronchospasm, respiratory failure, and laryngospasm, respectively. Complication rates were more frequent in elderly patients than younger patients and in those with uncontrolled asthma than those with controlled symptoms. The question persists whether the particular nature of cardiac surgery could put asthma patients at greater risk.

The most frequently used parameters for preoperative evaluation during the spirometric assessment are FEV_1 and FVC. In a number of studies comparing spirometric data and clinical findings, spirometric values were less valuable than patient history and physical examination [12]. Preoperative spirom-

etry values and postoperative complications do not always correlate. Furthermore, these values being normal does not indicate that the risk of postoperative complications will be low [8].

An essential step in the preoperative evaluation of asthma patients is to assess whether the disease is under control [13]. Poorly controlled asthma is a risk factor for the development of postoperative pulmonary complications [14]. However, the additional risk is lower in well-controlled asthma patients [15]. In previous studies, an increased risk of postoperative complications has not been reported in patients with controlled asthma. In a study of 706 asthma patients who had undergone surgical intervention, there was no increase in the frequency of postoperative death, pneumothorax, or pneumonia (5). Woods et al. [16] showed that while asthma is not an issue during elective surgeries, life-threatening bronchospasm may develop in emergency interventions if the disease is not controlled.

Hospitalization or the use of systemic steroids for asthma within 6 months increases further hospital admissions owing to asthma [17]. A study by Quezada et al. [18] showed that a history of asthma exacerbation within the last 12 months of follow-up was one of the strongest predictors of future exacerbations. A study by Chao-Shun Lin et al. [6] showed that a history of asthma-specific emergency department visits, hospitalizations, ICU stay, and use of systemic corticosteroids were independent contributing factors for postoperative complications in asthma patients. Surgical patients with emergency care for asthma 3 months preoperatively had nearly twice the risk of postoperative mortality compared with controls. Patients who were hospitalized for asthma in the 3 months preceding surgery had almost thrice the risk of developing postoperative pneumonia compared with controls. Cumulative asthma-specific hospital stays and ICU admissions because of asthma in the 24 months prior to surgery were associated with postoperative complications and mortality [6]. We found higher incidences of asthma attacks and sibilant rhonchi postoperatively in uncontrolled asthma patients than in partially controlled asthma patients and higher incidences in partially controlled asthma patients than in under control asthma patients.

While we have investigated many aspects of operative morbidity with asthma patients, studies with a larger cohort and a prospective design would be necessary to confirm our results and increase the understanding on the topic. The two groups in our study were not selected according to sex- and age-matched controls or propensity score analysis, and these, along with the retrospective nature of the study, constitute out limitations.

The presence of asthma did not affect mortality in asthma patients who have undergone CABG surgery, but it was observed to have an effect on morbidity, with particular risks for worsening of asthma symptoms. The control status of asthma did not have an effect on mortality, but the preoperative state of the disease had effects on the postoperative exacerbation of asthma.

To conclude, asthma did not affect mortality in asthma patients who have undergone CABG surgery, but it was observed to have an effect on morbidity, with particular risks for worsening of asthma symptoms. The preoperative evaluation of asthma patients scheduled for CABG surgery requires consideration of the control status of asthma. Further studies are needed to provide more evidence on the topic.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Dr Siyami Ersek Thoracic and Cardiovascular Surgery Research and Training Hospital (28001928-604.02/18.02.2016).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

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