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Potential risk factors for early large pleural effusion after coronary artery bypass grafting surgery.

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Abstract

Objective: In the current study, we investigated potential risk factors affecting early pleural effusion (PE) after coronary artery bypass grafting surgery.

Materials and methods: The research was carried out by a retrospective study design. The individuals were separated into two groups: PE group (n=102) and non-PE group (n=2786), respectively. The main outcome of the study was the presence or absence of PE. The demographic and clinical variables were predictor factors as follows: age, gender, smoking, diabetes mellitus, hypertension, obesity, body mass index, family history, chronic obstructive pulmonary disease (COPD), myocardial infarction, renal dysfunction, carotid artery stenosis, number of diseased coronary arteries including side branches, the presence of left main coronary artery (LMCA) stenosis (>50%), mitral annuloplasty, valve surgery, aneurysmectomy, atrial fibrillation, ventilation time, bleeding revision, length of stay in hospital, preoperative Left Ventricular Ejection Fraction (LVEF), cardiopulmonary bypass time, cross-clamp time, inotropes in intensive care and intra-aortic balloon pump (IABP). Multiple logistic regressions were used to predict PE based on the defined predictors.

Results: Number of diseased coronary arteries including side branches, carotid artery stenosis and length of hospital stay were significantly different between the groups ($p<0.05$) in univariate analyses. Based on these findings of multiple logistic regression, carotid artery stenosis, number of diseased coronary arteries including side branches (4 coronary arteries), ventilation time and length of stay in hospital were significantly associated with PE ($p<0.05$).

Conclusions: Carotid artery stenosis, number of diseased coronary arteries including side branches (4 coronary arteries), ventilation time and length of stay in hospital were associated with pleural effusions after coronary artery bypass grafting surgery. Modifications of the risk factors can reduce the potential risk of PE after surgical operation.

Keywords: Pleural effusion, Risk factors, Coronary artery bypass grafting surgery.

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Introduction

Coronary artery bypass grafting (CABG) surgery is performed using grafts of the saphenous vein (SVG), radial artery and/or the internal mammary artery (IMA). One of the complications of this surgery is pleural effusions (PEs) occurring in small amount in most of the patients or in larger quantities in some of the patients. In most patients undergoing CABG, left-sided pleural effusions occur in the first few days after the surgery. Fortunately, most of the small PEs undergoes gradual resolution following CABG surgery; however, in some certain patients it results in symptomatic enlargement [1-3]. Additionally, it is shown that the incidence of PEs at the time of discharge increases from 58% to 91% if the pleura is opened in patients (n=33 and 34, respectively) receiving IMA graft surgery [1,4]. Although effusions, characterized by dyspnoea, chest pain, tachycardia and fever, occur as early as the first 30 days following the operation, they may also be observed later than that time window. For example, approximately two months after CABG, a study reported that the incidence of PE's in the patients receiving IMA with and without pleurotomy was 9.1% (5 out of 55 patients) and 14.5% (3 out of 21 patients), respectively [5]. Another group of investigators searched the prevalence of pleural effusions in 349 patients by chest radiography at approximately 30 days after operation and found out that 63% had effusions. Although most of the effusions were small, 9.7% had a PE that occupied more than 25% of the hemi thorax. Additionally, prevalence of large effusions was higher in patients receiving IMA graft than those receiving SVGs (10.9 and 4.5%, respectively) [6].

There are some studies examining the risk factors associated with PE in children and adults [7-10]. These risk factors associated with PE included demographic and clinical features such as age, gender, longer lengths of stay in hospital, high-grade splenic injuries, body weight, duration of bypass, duration of endotracheal intubation, etc. The etiology of PEs is based on the geographical areas and the regional incidence of various diseases that lead to PEs. In the advanced countries, the main causes of PEs in mature individuals are pneumonia, cardiac failure, and malignancy [11,12]. In the current study, in addition to the risk factors reported in the aforementioned studies, we also investigated the other potential risk factors affecting early PE after CABG.

Materials and Methods

The current study was established in the department of cardiovascular surgery, Faculty of Medicine at Inonu University, Malatya, Turkey. 2888 patients with coronary artery disease, who had been admitted to our clinic for elective CABG surgery, were enrolled in our study. The research was carried out by a retrospective study design. PE was diagnosed based on the findings of chest x-ray. The individuals were separated into two groups: PE group (n=102) and non-PE group (n=2786), respectively. Individuals who had past beta-blocker or antiarrhythmic treatment, peripheral arterial diseases, sick sinus syndrome, heart failure (ejection fraction<35%), and a block of atrioventricular were excluded from the study. The main outcome of the study was the presence or absence of PE. The demographic and clinical variables were predictor factors as follows: age, gender, smoking, type 2 diabetes mellitus (DM), hypertension (HT), obesity, body mass index (BMI), family history, chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), renal dysfunction (chronic kidney injury) [13], carotid artery stenosis (CAS) (diagnosed with duplex ultrasound and angiography) [14], the presence of left main coronary artery (LMCA) stenosis, number of diseased coronary arteries including side branches (4 coronary arteries), mitral annuloplasty, valve surgery, aneurysmectomy, atrial fibrillation (AF), ventilation time, bleeding revision, length of stay in hospital, preoperative left ventricular ejection fraction (LVEF), cardiopulmonary bypass (CB) time, cross-clamp time, inotropes in intensive care and intra-aortic balloon pump (IABP). The chest tubes were taken out 2 days post operation. Chest tubes of the patients that were not taken out at day 2 postoperatively were excluded from the study. PE's were investigated by chest radiography at postoperative 4, 7, 15 and 19 days. The amount of early large PE in the patients was identified by measuring the fluid more than 25% of the hemi thorax [1] and occurring in the first 30 days following the operation. Patients regularly followed up in the outpatient clinic were asked whether they were suffering from shortness of breath or pleuritic chest pain. Chest radiography was performed if the patient was symptomatic. The size of the pleural effusion was estimated visually to determine the percentage of the hemi thorax occupied by pleural fluid using either lateral radiography or sonography. Patients with a pleural effusion occupying more than 25% of the hemi thorax on chest radiography or more than three intercostal space detected by ultrasonography were included in our study. Those neither without symptoms nor complete records were excluded. All patients underwent therapeutic thoracentesis. The initial effusions are largely bloody, with a median haematocrit over 5%. The possible cause of these effusions is trauma from the surgery and postoperative bleeding into the pleural space [1].

Surgical procedure

General anaesthesia was administrated to the patients, and conventional median sternotomy was implemented. On-pump CABG surgery was applied to each patient, and CB was settled by cannulating the right atrium and the ascendant aorta. Heparin (3 mg/kg) was implemented for anticoagulation. Activated coagulation duration was kept up for longer than 450 seconds, and a roller pump and non-pulsatile stream (2.4 L/m^2/min) were utilized. The patient was estranged to a core heat somewhere around 32°C and 34°C at the time of distal anastomosis performance, and was rewarmed to 36°C before weaning from CB. Cold blood cardioplegia was conveyed discontinuously through antegrade courses via the method. A final dose for "hot-shot" cardioplegia was delivered intermittently via antegrade routes and was administered quickly before the aorta was unclamped. An epicardial temporary pacemaker lead (FLEXON 3-0 temporary cardiac pacing lead, Syneture, Covidien, US) was set on the right ventricle. Left internal thoracic artery was employed as a graft for the left anterior descending artery and saphenous vein graft conduits were employed to bypass vessels other than the left anterior descending artery. Postoperatively, a little tube was utilized in all patients to drain the mediastinum. Chest tubes for draining the left pleural space were utilized in all IMA patients [15].

Statistical analysis

Qualitative variables were given as frequencies with percentages, while quantitative variables were expressed as mean ± standard deviation (SD) or median (25%-75%). Qualitative data were analysed by Pearson chi-square test, Fisher exact chi-square test or Yates' corrected chi-square test as appropriate. Quantitative data were analysed using independent sample t test or Mann Whitney U test as appropriate. All p-values<0.05 were considered significant. Multiple logistic regressions were employed to predict confounder-adjusted associations between dependent/outcome variable (PE) and the predictor factors described previously. Hosmer-Lemeshow test and Omnibus test of model coefficients were used for the evaluation of model significance.

Results

This study included 2888 individuals: 102 (3.5%) in PE group and 2786 (96.5%) in non-PE group, respectively. The demographic characteristics of the groups were presented in Table 1. Mean ages were 62.81 ± 10.01 for PE group and 60.91 ± 9.83 for non-PE group. In relation to the comparisons of the

demographic characteristics, there were no significant differences in age, gender, smoking, BMI, obesity, and family history between the groups (p>0.05).

Table 1. *The demographic characteristics of the groups.*

Variable	PE group (n=102)	Non-PE group (n=2786)	p
Age (years)	62.81 ± 10.01	60.91 ± 9.83	0.06
Gender			
Female	22 (21.57%)	689 (24.74%)	0.46
Male	80 (78.43%)	2096 (75.26%)	
Smoking			
Absent	51 (50%)	1212 (43.50%)	0.19
Present	51 (50%)	1574 (56.5%)	
Body mass index (kg/m^2)	26.30 ± 4.40	26.42 ± 8.82	0.77
Obesity			
Absent	87 (82.29%)	2273 (81.59%)	0.41
Present	15 (17.71%)	513 (18.41%)	
Family history			
Absent	78 (76.47%)	1977 (70.96%)	0.23
Present	24 (23.53%)	809 (29.04%)	

Table 2. *The clinical characteristics of the groups.*

Variable	PE group (n=102)	Non-PE group (n=2786)	p
Age (years)	62.81 ± 10.01	60.91 ± 9.83	0.06
Gender			
Female	22 (21.57%)	689 (24.74%)	0.46
Male	80 (78.43%)	2096 (75.26%)	
Smoking			
Absent	51 (50%)	1212 (43.50%)	0.19
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Present	15 (17.71%)	513 (18.41%)	
Family history			
Absent	78 (76.47%)	1977 (70.96%)	0.23
Present	24 (23.53%)	809 (29.04%)	

The clinical characteristics of the groups were tabulated in Tables 2 and 3. Based on the results, while number of diseased coronary arteries including side branches, carotid artery stenosis, ventilation time and length of stay in hospital were significantly different between the groups (p<0.05), DM, HT, COPD, renal dysfunction, the presence of left main coronary artery stenosis, mitral annuloplasty, valve surgery, aneurysmectomy, AF, bleeding revision, preoperative LVEF, CB time, cross-clamp time, inotropes in intensive care and IABP were not significantly different (p>0.05). The results of multiple logistic regression analysis were given in Table 4. Based on these findings, carotid artery stenosis, number of diseased coronary arteries including side branches (4 coronary arteries), ventilation time and length of stay in hospital were significantly associated with PE (p<0.05). Hosmer-Lemeshow test showed that the multiple logistic regression was fit well to the analysed data (p=0.42). Additionally, Omnibus tests of model coefficients were statistically significant (p<0.001).

Table 3. *The other clinical characteristics of the groups.*

Variable	PE group (n=102)	Non-PE group (n=2786)	p
The presence of left main coronary artery			
Absent	96 (94.1%)	2674 (96%)	0.31
Present	6 (5.9%)	112 (4%)	
Mitral annuloplasty			
Absent	102 (100%)	2769 (99.5%)	0.99
Present	0 (0%)	14 (0.5%)	
Valve surgery			
Absent	100 (98%)	2749 (98.7%)	0.38
Present	2 (2%)	35 (1.3%)	
Aneurysmectomy			
Absent	93 (91.2%)	2581 (92.8%)	0.67
Present	9 (8.8%)	200 (7.2%)	
Atrial fibrillation			
Absent	88 (86.3%)	2440 (87.6%)	0.81
Present	14 (13.7%)	346 (12.4%)	
Bleeding revision			
Absent	101 (99%)	2745 (98.5%)	0.99
Present	1 (1%)	41 (1.5%)	
Length of stay in hospital (days)	6.87 ± 2.04	7.93 ± 3.34	0.004
Preoperative Left Ventricular Ejection Fraction (%)	49.23 ± 10.52	49.18 ± 10.11	0.97
Cardiopulmonary bypass time (min)	91.91 ± 26.07	91.23 ± 28.24	0.87
Cross-clamp time (min)	76.44 ± 23.10	73.62 ± 21.73	0.37
Inotropes in intensive care			
Absent	88 (86.3)	2530 (90.8)	0.17
Present	14 (13.7)	256 (9.2)	

Intra-aortic balloon pump			
Absent	97 (95.1)	2718 (97.6)	0.18
Present	5 (4.9)	68 (2.4)	

Table 4. The results of multiple logistic regression analysis.

Factors	B	S.E.	p	OR	95% CI for OR	
					Lower	Upper
Carotid artery stenosis	0.931	0.284	0.001	2.54	1.45	4.43
Number of diseased coronary arteries including side branches (4 coronary arteries)	2.85	1.268	0.025	17.29	1.44	207.38
Ventilation time	0.019	0.008	0.018	1.02	1.01	1.03
Length of stay in hospital (days)	0.103	0.035	0.003	1.11	1.04	1.19
Constant	-3.341	0.432	<0.001			

CI: Confidence Interval; SE: Standard Error; OR: Odds Ratio.

Discussion

The current study examines many potential risk factors affecting early PE after CABG surgery. When evaluated clinically, PE is a common medical condition; however, the elaborate pathogenesis for the accumulation of pleural fluid has not been fully understood [16]. The management of PE is one of the medical challenges leading to an important cost for the patients and the system of health care. Many laboratory tests are employed in the differential diagnosis of PE; after all, no diagnosis has been put in an important contribution [17,18]. In the current study, the pathophysiology of PE may be related to the two main factors. Trauma in the course of surgery may cause to blood in the pleural space generating PE. Also, the operation could cause immunologic reactions to be the result of PE development [19]. Similarly, in this study, the possible reason of this PEs may be related to trauma from the operation. Causes for complicated PE are multifactorial. In addition, etiologic factors vary according to the study of units and regions [20]. Patients take the advice of doctors so late after the beginning of the symptoms; almost a large part of the studied patients had conditions that can induce immunosuppression [21]. Therefore, identification and taking control of potential risk factors associated with PE are so important to prevent the disease progression. In this context, the current study considers potential risk factors associated with early PE after CABG surgery. According to the findings of multiple logistic regression, the most relevant factor associated with PE was the number of diseased coronary arteries including side branches with 4 coronary arteries (OR=17.29; 95% CI=1.44-207.38). The variables related to PE in order of importance were carotid artery stenosis (OR=2.54; 95% CI=1.45-4.43), length of stay in hospital (OR=1.11; 95% CI=1.04-1.19), ventilation time (OR=1.01; 95% CI=1.01-1.03), respectively. A study reported that patients with chiefly left-sided PE might have a secret thoracic internal artery surgery and on-pump cardiac surgery [22]. This observation can elucidate the relationship between carotid artery stenosis and PE. There are various hypotheses in the explanation of PE. It could be cardiogenic or noncardiogenic, caused by acute pulmonary oedema after CB. Reperfusion injury in cold and ischemic pulmonary tissue generates oxygen free radicals that modify the vascular permeability. The increased vascular permeability resulting from these processes causes diffuse pulmonary oedema and pleural effusion [23]. In our patients, PE may be related to reperfusion injury. In general, pleural effusions caused by pulmonary oedema either from heart failure or from acute lung injury are bilateral and approximately equal in size [24]. In our patients did not present evidence of heart failure, and PEs have been usually unilateral. The post cardiac injury syndrome is usually manifested after the second or third week of surgery [25]. The lymphatic drainage from the pleural area could be postoperatively diminished, especially in patients receiving an IMA graft. This disruption could be expected to decrease the lymphatic clearance from the pleural space and result in the accumulation of pleural fluid [5]. We believe that this explanation does not explain the fluid accumulation in the left pleura due to our diligence in our cases. The presence of a chest tube could have led to a pleural inflammation and the development of the effusion [2]. In our cases, the lungs of our patients did not fully expand owing to prolonged intubation of our patients and this condition may be due to early non-mobilization of the patients. The performance of pleurotomy could have led to the accumulation of pleural fluid. The trauma during cardiac surgery could have damaged and pleural fluid formation was increased. Our study provides support for the contention that pleural effusions are related to the performance of pleurotomy [5]. PE could be associated with the pericardial inflammation. Likelihood happens that the pericardial liquid streams straight into the pleural area over fenestrations. The development of PE could be attributed to the presence of atelectasis. PE's are one of the etiological factors associated with atelectasis. Other etiological factors are type and duration of general anaesthesia, type and duration of surgery, underlying lung sickness, underlying neuromuscular ailment, chronic systemic illness or debility, obesity, age, etc. [26] One of the causes explained above related to PE could take place in our cases. A study investigated the potential risk factors for prolonged PE, and reported that the risk factors for prolonged PE were sex, age at repair, body weight, duration of bypass, low oxygen saturation before the operation, wound infection after operation, time for endotracheal intubation, duration of stay in hospital, and Nakata index [27]. In the current study, duration of stay in hospital was a significant factor associated with PE as reported in the previous study. In this respect, the findings of the aforementioned study were in agreement with our study. As a result, carotid artery stenosis, number of diseased coronary arteries including side branches (4 coronary arteries), ventilation time and length of stay in hospital were associated with pleural effusions after coronary artery bypass graft surgery. Modifications of the risk factors can reduce the potential risk of PE after surgical operation.

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