CAN PROGRESSION OF SUBSEQUENT HYPOXIA BE ESTIMATED BY PREOPERATIVE PULMONARY FUNCTION TESTS AFTER CORONARY BYPASS GRAFTING ?

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This study has been undertaken to determine the relationship between the progression of postoperative hypoxia in patients who underwent coronary bypass operation and the parameters to be taken into consideration for this purpose.
Onehundred consecutive patients who underwent elective coronary bypass operation were included in the study. Blood gas samples from all subjects were taken at 12, 24, 36 and 48 hours after extubation. The patients were divided into 2 groups according to their blood gas measurement. Postoperative blood gas evaluation were divided into (non-hypoxic group) $PaO_2 \geq 75$ mmHg and $PaO_2 \leq 74$ mmHg on the basis of two or more measurements (hypoxic group).
No significant difference was found between BSA, EF, preoperative PaO_2, PCO_2, FVC, FEV1, FEV1/FVC, FEF 25-75%, number of grafts, X-clamp time, ventilator duration and duration of stay in intensive care unit, but a statistically significant relationship was detected between PEF values (p=0.004) and CPB duration (p=0.034).
The number of patients that have FEF25-75% ≤ 74% and PEF≤ 74% were more in the hypoxic group than the non-hypoxic group (p=0.016 and p=0.000). The number of patients that have a CPB time longer than 90 minutes is significantly higher in the hypoxic group compared to the other group (p=0.002).
Since deterioration in pulmonary function after CABG operations is of great importance, preoperative and perioperative parameters should be well evaluated. We found that a reduction in FEF25-75% and PEF values is more important than preoperative FVC, FEV1, FEV1/FVC values in determining postoperative hypoxia. Shortening the CPB time during perioperative period is important in reducing the deterioration of postoperative pulmonary function.

Key words: Coronary Artery Bypass Grafting, Postoperative Hypoxia, Pulmonary Function Test

It is important to estimate the complications that may develop after open-heart surgery. Most of the patients who underwent coronary bypass surgery, have a history of smoking, that also may play a role in progression of lung disease. For this reason, pulmonary function tests should be performed before the operation and the pulmonary complications likely to develop postoperatively should be estimated beforehand.

The deterioration of preoperative pulmonary status after open-heart surgery may be responsible for postoperative respiratory complications. In patients with impaired pulmonary functions; the risk of developing pulmonary complications is higher and the duration of stay at intensive care unit (ICU) is longer [1-3]. It takes longer for respiratory functions to heal in obstructive diseases compared to restrictive diseaes.

Many studies have realized that the respiratory problems that may develope after an open-heart surgery can be anticipated in the preoperative period. The results have indicated that some pulmonary function tests (PFT) in the preoperative period can give predictive information about the postoperative period, whereas some have no utility in terms of being informative [4-10].

The present study was undertaken to determine the relationship between the postoperative development of hypoxia and the preoperative respiratory function tests in patients that had coronary bypass surgery, also to determine the parameters to be considered for this purpose.

MATERIAL AND METHODS

A total of 285 patients were retrospectively screened for this study and 185 of them did not meet the inclusion criteria. Approval to conduct the study was obtained from Trakya University Research Ethical Committee and all patients gave informed consent prior to participation.

The preoperative demografic characteristics, cardiac performances, respiratory function tests, arterial blood gas analysis results and the postoperative intensive care data of the patients were investigated in detail. The ejection fraction obtained by the left ventriculography was used to evaluate the cardiac functions. The PFTs were performed at the respiratory physiology laboratory. The PFTs of all the cases were repeated for 3 times on the spirometer (Sensormedics 2400, USA) by the same technician and the highest values were considered. The patients that had emergency CABG surgery, valvular surgery, combined cardiac operations (CABG +valve), beating heart operations, preoperatively taking bronchodilator treatment and developed postoperative neurologic and renal complications were excluded (n=185). The remaining were divided into 2 groups as the patients who have $PaO_2 \geq 75$ mmHg in postoperative blood gas evaluation (non-hypoxic group, n=22) and the patients who have $PaO_2 \leq 74$ mmHg in two or more measurements (hypoxic group, n= 78). The demographic characteristics of the two groups, the parameters of the pulmonary function tests and the numerical variables were compared.

Main parameters measured by PFT include the vital capacity (VC), the peak expiratory flow (PEF), the forced expiratory flow at the first second (FEV1) and the maximum mid-expiratory flow (FEF25-75%). FVC is the volume of air exhaled into the spirometer with maximum expiratory effort as rapidly and as completely as possible after inspiration maximally to the total lung capacity. FVC increases in obstructive airway diseases. FEV1 is the volume of air at first second of forced expiration and gives general information about small airways. Normally 80% of volume inspired by vital capacity is expired at first second. This is also dependent on the patient's cooperation and effort. FEV1/FVC ratio (Tiffeneau ratio) is normally above 75%. This ratio is reduced in obstructive airway diseases. FEF 25-75% is the maximum mid-expiratory flow velocity. It is the air flow velocity of 25-75% volume expired during forced expiration, it gives general information about the flow in medium and small airways. FEF 25-75% is more sensitive than FEV1 in showing early airway obstruction since its measurement is not effort dependent. It decreases in early period of obstructive diseases. PEF is the maximal airflow velocity during forced vital capacity maneuver. It gives information about the diameter of central airways and activity of expiratory muscles in healthy individuals; like FEV1 it is also effort dependent.

Surgical Tecnique:

Patients were premedicated by 0.1 mg/kg morphine and 0.3-0.4 mg scopolamine administration. Anesthesia induction was performed by 50 μg/kg fentanyl and 0.8 mg/kg pancuronium injection. Anesthesia was continued by oxygen and sevoflurane administration during the operation.

After median sternotomy internal mammary artery (IMA) was prepared with its pedicule; the ascending aorta and the right atrium was cannulated. Moderate systemic hypothermia (28±20C) and topical hypothermia were performed. Cardiopulmonary bypass (CPB) was applied by using a membrane oxygenator (Adult Hollov Fibre Oxygenator, D708 Simplex III Dideco inc, Mirandola, Italy) and a roller pump (Stöckert Inst, Munich, Germany). Induction of cardioplegia was applied by cold crystalloid cardioplegic solution through the root of aorta, continued with 400 ml of cold blood cardioplegic solution in every 20 minutes via an antegrade cannula. Mean arterial pressure was maintained during CPB at 60-70 mmHg.

The cross clamp was removed after distal anastomoses were completed. After fibrillation, defibrillation was done with 10 or 20 joules. Proximal anastomoses were completed after the side clamp was placed on the aorta.

Two drains were placed into the mediastinum from the subxiphoid region. An additional drain was placed to the thorax space if pleura was opened during LIMA harvesting. Mediastinal drains were removed on the first postoperative day, thorax drains were removed if the amount of drainage is not exceeding 100 ml/day.

Respiration of these sedatized-curarized patients was assisted at postoperative period. (controlled mandatory ventilation) (Evita 4 ventilator, Drager, Germany). Meanwhile tidal volume was adjusted to 10 ml/kg, respiration to 12/min, oxygen fraction (FiO_2) to 40%, ratio of inspiration/expiration to 0.50 and positive end-expiratory pressure (PEEP) to 5 cmH2O. When the effect of curare was terminated and spontaneous breathing started, we commenced supplementary intermittent mandatory ventilation (SIMV). Then supplementary respiration was adjusted to 10 per minute, in course of time we reduced respiratory support gradually and the patient was extubated.

In the preoperative period, blood gas samples were taken from all patients after 15 minutes of regular room air breathing in semifowler position. After extubation, blood gas samples for the research were taken at the intensive care unit 2 hours after analgesic injection (Diclofenac 1.5 mg/kg) in semifowler position. Oxygen support (with oxygen mask) was ceased 30 minutes before taking the blood gas sample. Blood gas samples were taken from all patients at 12, 24, 36 and 48th hours after extubation for standardization.

Respiratory exercises were performed to all patients with "volumetric incentive spirometry" both preoperatively and postoperatively.

Statistical Analysis:

All data were evaluated by SPSS program (Version 9.0;SPSS Inc, Chicago, IL, USA) for statistical analysis. Results were given as the mean and the standart deviation of mean.

The mean of each parameter was taken as a reference point in conversion of numerical data into catagoric data. Q-square test was used to compare catagoric variables in groups. Mann-Whitney U test and Student's t-test were used after controlling the distribution of noncategoric data with Kolmogorov-Simirnov test.

The statistical significance value was taken as $p<0.05$.

RESULTS

Both groups were similar in age, body surface area, EF, period of smoking, preoperative PaO_2 and PCO_2 values, number of grafts and x-clamp time (Table 1). The number of blood transfusions did not statistically differ between groups (p=0.542). History of smoking was present in 15 patients in non-hypoxic group, 54 patients in hypoxic group and LIMA was

Table 1. Distribution of numerical data among groups in the study.

	Non-hypoxic group (n= 22)	Hypoxic group (n= 78)	p value *
Age (year)	55.6 ± 9.6	57.5 ± 10.4	0.433
BSA (m2)	1.7 ± 0.1	1.8 ± 0.1	0.322
EF (%)	56.5 ± 16.1	58.5 ± 15.8	0.608
Smoking (years)	56.8 ± 23.5	59.5 ± 19.3	0.702
Preop PaO_2 (mmHg)	91.8 ± 9.5	87.9 ± 9.0	0.080
Preop$PaCO_2$ (mmHg)	34.8 ± 5.3	37.1 ± 5.0	0.065
FVC (%)	93.1± 11.5	88.4 ± 13.5	0.142
FEV1 (%)	95.1 ± 12.7	88.4 ± 13.5	0.056
FEV1/ FVC (%)	94.7 ± 10.2	100.5 ± 15.5	0.107
FEF %25-75 (%)	89.7 ± 22.3	80.1 ± 28.0	0.143
PEF (%)	82.0 ± 17.6	68.3 ± 19.7	0.004
Number of grafts	2.0 ± 0.5	2.3 ± 0.7	0.092
CPBT (min)	77.3 ± 20.8	90.0 ± 33.1	0.034
X-clamp time (min)	43.0 ± 12.2	49.4 ± 18.9	0.065
Blood transfusion (units)	4.3 ± 2.1	5.1 ± 1.8	0.542
PaO_2 12th hour	79.2±11.63	64.7±8.01	0.000
PaO_2 24th hour	79.7±9.23	63.4±8.34	0.000
PaO_2 36th hour	82.4±8.03	64.7±8.72	0.012
PaO_2 48th hour	90.8±9.6	68.3±7.84	0.273
Ventilator period (min)	806.0±276.0	958.0 ± 396.0	0.096
Stay in ICU (days)	2.7 ± 0.8	3.1 ± 1.1	0.102

*:Student t test

BSA: Body surface area, EF: Ejection fraction, PaO_2: partial oxygen pressure in arterial blood, $PaCO_2$: partial carbondioxide pressure in arterial blood, FVC: forced vital capacity, FEV1: the volume expired in the first second of the forced vital capacity. FEF25-75% : the forced expiratory flow between 25% and 75% of vital capacity, PEF: peak expiratory flow, CPBT: cardiopulmonary bypass time, X-clamp: cardiac ischemia time, LIMA: left internal mammary artery, AMI: acute myocardial infarct.

used in 16 patients in non-hypoxic group and 52 patients in hypoxic group.

Investigating the preoperative PFTs, it was detected that preoperative PEF values were significantly lower in the hypoxic group compared to the non-hypoxic group (p=0.004). FEV1 values in the hypoxic group were lower compared to the hypoxic group, but the difference was not statistically significant (p=0.056). It was detected that CPB time was longer in the hypoxic group (p=0.034).

Postoperative PaO_2 levels reduced significantly especially at the 12th (p=0.000), 24th (p=0.000) and 36th (p=0.012) hours in the hypoxic group, also it was similar between the groups at the 48th hour (p=0.272) (Table 1). No statistically significant difference was detected between the groups in terms of ventilatory period (p=0.096) and stay at intensive care unit (p=0.102). In the routine ECG, CK-MB and Troponin-I follow-up of the patients at the intensive care unit in the postoperative period, perioperative MI was detected in one patient from each groups. In both patients, the ventilatory period (1245 minutes in patient from the hypoxic group and 1048 minutes in patient from the non-hypoxic group) and the stay at the intensive care unit (4.1 days in patient from the hypoxic group and 3.5 days in patient from the non-hypoxic group) were over the group average, and the postoperative PaO_2 values were lower than 75 mmHg.

Table 2. Distribution of categorical variables and results of comparison

	Non-hypoxic group (n= 22)	Hypoxic group (n= 78)	p value *
Male sex	21	68	0.448
Female sex	1	10	
BSA≥ 1,72 (m2)	13	63	0.069
BSA ≤ 1,71 (m2)	9	15	
EF≥ 50%	17	57	0.904
EF≤ 49%	5	21	
Preop PaO2 ≥75mmHg	21	75	1.000
Preop PaO2≤74mmHg	1	3	
Preop PaCO2≥44mmHg	21	76	0.530
Preop PaCO2≤ 45mmHg	1	2	
FVC ≥75%	22	69	0.200
FVC ≤74	0	9	
FEV1≥75%	22	66	0.063
FEV1≤75%	0	12	
FEV1/ FVC≥75%	21	78	0.220
FEV1/ FVC≤75%	1	0	
FEF 25-75%≥75%	18	39	0.016
FEF 25-75%≤74%	4	39	
PEF≥75%	17	21	0.000
PEF≤74%	5	57	
CPBT≥ 90	2	38	0.002
CPBT≤89	20	40	
X-clamp time≥ 60 min	2	20	0.145
X-clamp time≤ 59 min	20	58	
Ventilator period ≥ 925 min	9	45	0.249
Ventilator period ≤ 924 min	13	33	

*: q-square test

BSA: Body surface area, EF: Ejection fraction, PaO2: partial oxygen pressure in arterial blood, PaCO2: partial carbondioxide pressure in arterial blood, FVC: forced vital capacity, FEV1: the volume expired in the first second of the forced vital capacity. FEF25-75% : the forced expiratory flow between 25% and 75% of vital capacity, PEF: peak expiratory flow, CPBT: cardiopulmonary bypass time, X-clamp: cardiac ischemia time.

Table 2 shows the evaluation of the categoric data formed by taking the mean point of the numerical data. Here, it was detected that the number of patients who have FEF25-75% ≤ 74 % and PEF ≤ 74 % were significantly more in the hypoxic group compared to the non-hypoxic group ($p=0.016$ and $p= 0.000$). The number of patients who have a CPB time ≥ 90 minutes was significantly more in the hypoxic group compared to the other group ($p=0.002$).

DISCUSSION

Pulmonary problems are one of the most common complications after CABG operations. Even though they are caused by anesthesia and cardiopulmonary bypass methods, end even if the preoperative evaluation and visualization methods, infection control and physiotherapy approach are utilized, pulmonary complications still occur in high rates after cardiac surgery [5,11-15].

The factors that may predispose to respiratory problems after cardiac surgery may be classifield in to three groups as pre, peri and postoperative. The respiratory problems that develop after cardiac surgery are the results of the combined effect of those factors. The preoperative factors are age, female sex, emergency operation, left ventricular dysfunction, reoperation, DM, low body surface area and poor respiratory function test. Perioperative factors are the long duration of operation, the size of the surgical injury, the negative effects of median sternotomy on the respiratory mechanism, longer CPB time, inadequate revascularization and inadequate myocardial protection. The postoperative factors are persistent atelectesia because of insufficient rehabilitation, diaphragmatic dysfunction due to phrenic nerve injury and massive blood transfusions [11,15-18].

Vital capacity, inspiratory capacity, functional residual capacity, total lung capacity and pulmonary diffusion capacity are reduced after cardiac surgery, it takes approximately four months for a patient to reach preoperative levels. The constructive changes after median sternotomy may cause a restrictive type pulmonary dysfunction and this may continue even for weeks after the operation [4,19].

Prevention of pulmonary complications has a direct effect on hospitalization period and mortality rates. So, it is important to estimate the pulmonary complications before the operation in high risk patients to plan the operative strategy and inform patients.. A careful medical history of the patient and complete physical examination is necessary. Other preoperative methods are the radiologic interventions of respiratory system, pulmonary function tests and blood gas analysis in room air.

Pulmonary function test is the commonly used technique since it is a non-invasive, easily performed method and doesn't increase the cost. Instead of the caseness of this technique, it requires high patient cooperation which may lead to misinterpretation of the results. Since performance of the test is directly correlated with the patient's cooperation, its results also the depend on educational level of the population.

We may have information about airway resistance and structure of lung parenchyme with the aid of pulmonary function tests. Pulmonary function tests are performed in the preoperative period to patients who will have CABG surgery to anticipate pulmonary complications after surgery in most of the cardiovascular surgery clinics. The basic parameters used in differentiation of obstructive and restrictive diseases are VC and FEV1. Main parameters used for this reason include FVC, FEV1 and FEV1 / FVC ratio. FEF25-75% and PEF values are usually not considered or omitted [1,4,5,12,20].

Postoperative hypoxia in the postoperative period has a great importance in cardiac surgery performed patients. Early diagnosis of hypoxia is important since it may predispose to myocardial ischemia and infarction in the state of increased oxygen demand.

Our aim in this study is to review factors affecting low PaO_2 levels in a series of blood gas analysis follow-up at intensive care unit after extubation of patients who had coronary bypass surgery. Nasal O_2 (3-5 L/min), respiratory physiotherapy and expectorant treatment (N-acetyl cysteine) were commenced to patients who have low PaO_2 levels in order to prevent the progression of hypoxia and pulmonary complications.

It has been shown that alveolo-capillary gas exchange is reduced at the postoperative period in patients who had coronary bypass surgery. The possible reasons are the decreased functional residual capacity and the pulmonary compliance, increased capillary shunts, increased alveolocapillary permeability. General anesthesia, surgical injury, median sternotomy, CPB, pleural effusion and the diaphragm dysfunction play important roles in those changes. The effect of preoperative risk factors increase, if myocardial protection is inadequate, intraoperative complications occur, myocardial revascularization is incomplete or reoperation is performed [13,20-24]. Pulmonary complications resulting from CPB are reduced with the widely used beating heart technique in the last decade [12,19].

Although median sternotomy impairs pulmonary functions, it is still the most commonly used method since it provides excellent exposure. In the early postoperative period sternotomy may cause impaired pulmonary mechanics, pleurotomy and pain and decreases in FEV1 and FVC. After the CABG there's approximetely 30-50% reduction in FEV1 and forced residual capacity (FRC) and they reach their basal levels nearly after 6 weeks [1,20].

Another parameter impairing the pulmonary functions is CPB. In the early period of CPB, complement activation and formation of C3a and C5a are increased. The inflammatory response commenced by the complements result in increased permeability of alveolocapillary membrane. Serum and macromolecules accumulate at interstitium and alveolar spaces. The positive fluid balance at the end of the operation is a result of increased extravascular fluid in lungs. Since the blood gas cells contact with the synthetic surfaces during CPB, neutrophils are activated. Activated neutrophiles provoke a pulmonary injury at the level of interstitium and endothelium. Leukocyte migration occuring in lung tissue enhances the amount of shunt; so that permeability of alveolocapillary membrane is increased. The fluid movement between intravascular and extravascular compartments in lung tissue is related to level of hemodilution, oncotic pressures and the endothelial integration at pulmonary vascular bed. As a result of the general inflammatory response, macromolecules penetrate into the interstitium and contribute to factors impairing pulmonary functions [15].

In this study, CPB time was found to be significantly longer in the hypoxic group and this showed the direct relation between postoperative hypoxia and CPB time once again.

Althouh the major factors affecting long CPB time are the number of grafts and cross-clamp time; in our study we found no significant statistical difference between the number of grafts and cross-clamp time. Since we continue CPB till body temperature reaches 360C (rectal) together with hemodynamic stabilization, CPB times were found to be longer unproportional to the number of grafts and cross-clamp time.

There are many studies in literature for respiratory problems after CPB in the preoperative period. Some of these studies showed that the preoperative pulmonary function tests can give simulatory information about postoperative period, some bring out that this is not beneficial [4-10]. In this study, we considered the values which Spivach et al [5] accepted as abnormal (FVC, FEV1, FEV1/FVC<75%, PaO2<75 mmHg, PaCO2>45 mmHg and LVEF<50%). Previous studies especially mentioned the reduction in FVC, FEV1 and FEV1/FVC values, but they don't include any information related to FEF25-75% and PEF values. Although FVC, FEV1 and FEV1/FVC values are normal, impairment in FEF25-75% and PEF values which show flow rate can be demonstrated.

In this study; it was detected that the number of patients which have FEF25-75% ≤ 74 % and PEF ≤ 74 % were significantly more in hypoxic group compared to non-hypoxic group ($p=0.016$ and $p= 0.000$), this demonstrated the importance of FEF25-75% and PEF values in estimating postoperative hypoxia. This shows patients who has low FEF25-75% and PEF levels in pulmonary function tests preoperatively have higher risks to develope hypoxia in the postoperative period.

The volumetric incentive spirometry is used in the reduction of postoperative atelectesia and the respiratory problems. Crowe et al [25] stated that the use of incentive spirometry is not superior in decreasing pulmonary complications. Although we used volumetric incentive spirometry in all patients both preoperatively and postoperatively, 78 patients had low PaO_2 postoperatively. Our results support the conclusion of Crowe et al.

Can preoperative arterial blood gas analysis results help us in defining the possible development of postoperative hypoxia? In this study, although we couldn't find out any statistically significant relation between preoperative PaO_2 and $PaCO_2$ levels, development of postoperative hypoxia in most of the patients showed us that preoperative arterial blood gas analysis results are not adequate for estimating postoperative hypoxia. Since our study includes a limited number of patients, in order to decide a certain conclusion, results of larger series are necessary.

Although blood transfusion is a well-known risk factor in the development of postoperative pulmonary complications [16], we compared postoperative low PaO_2 levels and the number of blood transfusions in units and we couldn't find any significant difference among groups. Lichtenberg et al [12] showed in patients undergoing operation with using CPB that the decrease in PaO_2 levels is usually observed at the first postoperative day. In our study, although the PaO_2 levels were significantly low at 12th, 24th and 36th hours during the postoperative period, statistical difference disappeared at 48th hour.

In conclusion, since impairment of the pulmonary functions is of great importance after CABG surgery, pre- and perioperative determinants should be decided. We suggest that the reduction in preoperative FEF25-75% and PEF values more objectively determined the postoperative hypoxia. Additionally, shorter durations of CPB may contribute to decreased postoperative impairment of pulmonary functions.

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