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Original Article

Coronary Bypass Surgery in Patients with Pulmonary Hypertension: Assessment of Early and Long Term Results

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Purpose: We aimed to evaluate the effects of preoperative pulmonary hypertension (PH) on early and long term results in patients undergoing coronary bypass surgery and the effects of coronary bypass surgery on PH.
Methods: Among 2325 patients who underwent elective isolated coronary artery bypass surgery between March 2003 and March 2012, 287 patients with high preoperative pulmonary arterial pressure (PAP) ≥30 mmHg were examined. Patients' data were obtained by retrospective examination of our clinic's database. 69 patients who had complete parameters included in the study.
Results: There was no increase in the New York Heart Association (NYHA) functional classification 84% of cases. Preoperative and postoperative values of the mean ejection fraction and mean PAP of patients was respectively 45.28 ± 9.67 (25–65), 46.03 ±12.4 (20–65) (p = 0.447), 36.67 ± 6.81 (30–60) mmHg, 37.81 ± 10.07 (20–70) mmHg (p = 0.378). The late mortality of cases was 5.79%. In our study, during 33.9 ± 17 (9–100) months follow up period, life expectancy was calculated as 94.7 months.
Conclusion: Preoperative evaluation of these patients for appropriate medical treatment at peroperative and postoperative period, coronary bypass can be performed with low morbidity and mortality rates. In the late period after surgical revascularization PH showed no significant change and had no adverse effect on quality of life.

Keywords: Pulmonary hypertension, coronary artery bypass surgery, Outcomes

Introduction

Pulmonary hypertension (PH) is one of the main causes of increased mortality and morbidity rates in open heart surgery. Left heart disease is probably the most frequent cause of PH.[1)] Left-sided ventricular or valvular diseases may lead to an increase in left atrial pressure, and the passive backward transmission of this pressure may result in increased pulmonary arterial pressure (PAP).[2)] Despite intensive postoperative medical treatment, an increase is observed in mortality and morbidity rates following coronary bypass surgery in patients with PH and right heart failure.[3,4)]

PH has a significant effect on right ventricular afterload. Various studies have shown that patients with right ventricle dysfunction display higher rates of early perioperative mortality and poor long term survival.[5,6)]

In this study, we investigated the effect of preoperative PH on the early- and long term results of patients who underwent isolated coronary artery bypass surgery, as well as its effect on the quality of life and the changes in

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PH after surgical revascularization. This study was conducted as a retrospective study, and our aim was to evaluate early- and long term results in order to determine 9-year survival rates.

Materials and Methods

Following the approval of the ethics committee (research protocol code: 2012/70), this study was conducted at the Cardiovascular Surgery Department of the Medical Faculty of Inonu University. Among 2325 patients who underwent elective isolated coronary artery bypass surgery between March 2003 and March 2012, 287 patients with high preoperative PAP ≥30 mmHg were examined. Preoperative, early postoperative (≤30 days) and late postoperative (≥30 days) data were obtained by retrospective examination of our clinic's database, and 69 patients with complete data who were on follow-up were included in the study. Parameters such as pulmonary arterial pressure, ejection fraction, New York Heart Association (NYHA) functional classification and the presence of arrhythmia were evaluated in both the preoperative period and of the final examination of the postoperative period.

The exclusion criteria of the study were as follows: Primary (organic) valve pathology; lung pathology; connective tissue diseases; hematologic, metabolic (thyroid), and systemic (sarcoidosis, vasculitis) disorders; chronic kidney failure; surgical procedures except coronary bypass (valve surgery, aortic surgery, left ventricle aneurysmectomy); off-pump coronary bypass.

Forty-four of the patients (63.8%) were male, while 25 patients (36.2%) were female. The mean age of the patients was 63.84 (45–79). The mean follow-up period was 33.9 ± 17 (9–100) months.

Anesthesia

Patients were monitored following their transfer to the operating room. A pulse oximetry probe was placed and used to monitor peripheral arterial oxygen saturation. A 20 G branule was placed on the right radial artery to monitor systemic arterial pressure and arterial blood gas. Anesthesia was induced with 2% lidocaine (1 mg/kg), 0.2–0.3 mg/kg of midazolam, 5 μg/kg fentanyl, and 0.1 mg/kg vecuronium. All patients were manually respirated, then intubated by monitoring full muscle relaxation, and finally connected to a mechanical ventilator. Anesthesia was continued with 10–30 μg/kg fentanyl and 0.1–0.3 mg/kg/hour midazolam, depending on the hemodynamic condition. For antibiotic prophylaxis, 1 g of cefazolin sodium was administered intravenously (i.v.) before surgical incision.

Surgical Technique

All procedures were performed under cardiopulmonary bypass (CPB) by using median sternotomy. A roller pump, a non-heparin coated oxygenator, a polyvinylchloride tubing set, and a two-step venous cannula were used for cardiopulmonary bypass. Mild systemic hypothermia (33–34 °C) was induced, and a 2.4 L/min/m^2 non-pulsatile pump flow was employed. Hematocrit was maintained between 22–25% during cardiopulmonary bypass, and mean arterial was pressure was kept constant between 50–70 mmHg. Anticoagulation was provided by heparin administration immediately prior to CPB (active clotting time >480s. Antegrade and retrograde cold blood cardioplegia were used for myocardial protection. Warm blood cardioplegia was administered before removing the aortic cross-clamp. Internal mammarian artery (IMA) graft was preferred for left anterior descending (LAD) artery anastomosis in all patients. In cases where the IMA graft was not suitable, a saphenous vein graft was used instead. In suitable cases of multiple coronary artery disease, radial artery and/or saphenous vein grafts were employed in addition to the IMA graft. Distal anastomosis was performed with a 7-8/0 prolene suture under cross-clamp, and proximal anastomosis was performed with a 6/0 prolene suture under cross-clamp.

Before the removal of the cross-clamp, all patients were administered with methyl prednisolone, theophylline ethylenediamine, and acetyl cysteine. During postoperative intensive care follow-up, patients received i.v. nitroglycerine infusion (high dose to the maximum tolerated level) and acetyl cysteine (in intensive care; i.v., and then per oral). Methyl prednisolone, theophylline ethylenediamine, acetyl cysteine, and lidocaine were administered to the patients who were to be extubated. Following extubation, patients received lung care with postural drainage. Treatment with nebulizers, bronchodilators and vapor were performed whenever necessary.

Data Collection and Definitions

The patients' preoperative and final examination results (anamnesis, physical examination, electrocardiography, thoracography, transthoracic echocardiography) were evaluated. As such, parameters such as the patients'

pulmonary arterial pressure, ejection fraction, pleural effusion, pericardial effusion, NYHA functional classification (FC), and arrhythmia were examined both preoperatively and postoperatively.

Patients were considered as having chronic kidney failure (CKF) in case they were affected by an irreversible pathological condition characterized by loss of the kidneys' ability to maintain homeostasis. Preoperative renal insufficiency was defined as a serum creatinine level ≥1.5 mg/dL prior to coronary artery bypass surgery.[7]

Patients are generally considered as having PAH when their mean PAP exceeds 25 mmHg at rest, and 30 mmHg during exercise.[8] Transthoracic echocardiographies were performed by the Cardiology Department of the Medical Faculty on the left lateral decubitus, the parasternal long axis, the parasternal short axis and the apical four chamber of the patients. Until March 2009, the echocardiographies were performed using an HDI 5000 CV instrument (ATL, Philips, Bothell, USA); and starting from March 2009, an IE33 instrument (Philips) was used for performing the echocardiographies. Pulmonary arterial pressure was calculated using the modified Bernoulli equation, which factors in the tricuspid regurgitation.

The examiner made the best effort to carefully and accurately measure pulmonary arterial pressure. To this end, the acoustic window which allows the best imaging of tricuspid regurgitation in color doppler echocardiography, (and where the angle between ultrasound bundle and flow direction was as close to zero as possible) was preferred. When different pulmonary arterial pressures were measured in different echocardiographic windows, the higher value was recorded as the correct value.

Statistical Analysis

The SPSS 16.0 package program (SPSS Inc. Chicago, Illinois, USA) was used for the statistical analyses. Estimated survival rate was calculated using Kaplan-Meier method (95% confidence interval). Continuous variables were compared using the unpaired student's t-test. Data were shown as mean ± standard deviation, numbers, and percentages. P values ≤0.05 were considered as statistically significant.

Results

The mean Euroscore value was 4.49 ± 3.21 (0–14). Forty two (60.9%) of the patients had a history of myocardial infarction, while 16 (23.2%) of the patients had complaints relating to unstable angina. Percutaneous coronary intervention (PCI) procedure was performed in 14.9% (n=10) of the patients.

The mean body-mass index (BMI) was 26.83 ± 4.20 (18–37) kg/m^2, and 24.6% (n = 17) of the patients were identified as being obese. Thirty-five (50.7%) of the patients had a history of smoking at least 1 pack of cigarette per day for the last 10 years, yet lacked any findings or symptoms relating to chronic obstructive pulmonary disease (COPD). Carotid artery stenosis was present in 13% (n = 9) of the patients; however, carotid artery stenosis did not require intervention in any of the patients.

The demographic characteristics of the 69 patients who were included into the study are shown in **Table 1**.

The mean number of bypass surgeries for the patients was 2.25 ± 0.83 (1–5), while the mean cardiopulmonary bypass duration and the mean cross-clamp duration were 80.66 ± 22.92 (27–128) min and 67.88 ± 19.59 (19–105) min, respectively. The preoperative data of the patients are shown in **Table 2**.

The most commonly encountered problem during the early postoperative period (≤30 days) was atrial fibrillation (14.4%). All patients (14.4%) received i.v. amiodarone infusion for 24 h while in the intensive care unit, and treatment was continued with per oral amiodarone once a normal sinus rhythm was obtained.

During the early postoperative period at the intensive care unit; 9 (13%) of the patients required inotropic support, and intra-aortic balloon pump (IABP) was performed in one (1.4%) of the patients. Preoperative renal functions were normal in all of the patients, while temporary early-stage renal dysfunction was observed in 5.8% of the patients.

The mean duration of mechanical ventilation was 8.14 ± 4.9 (3–40h). Long stay at the intensive care unit (≥6 days) was observed for 2.9% of the patients, while delayed duration of mechanical ventilation (≥24 h) was observed in 1.4% of the patients. Two (2.9%) of the patients were transferred to the intensive care unit due to respiratory failure during monitoring. The mean duration of follow-up at the intensive care unit was calculated as 2.83 ± 1.19 (1–8) days.

The mean drainage volume from the thorax and mediastinum tube drainage systems was 376.50 ± 182.29 (125–900) cc. Revision due to bleeding did not occur.

Deep vein thrombosis, pneumonia, and gastrointestinal system complications were not observed. Early mortality was not observed within our case series. The mean duration of hospitalization was 7.65 ± 3.26 (6–32) days.

Table 1 Demographical data of all patients

	Patients (n)	(%)
Gender (Female)	25	36.2
Unstable angina	16	23.2
Current smoker	35	50.7
Diabetes Mellitus	18	26.1
Hypertension	32	46.2
Obesity	17	24.6
CAD family history	31	44.9
Previous MI	42	60.9
Previous PCI	10	14.49
Hyperlipidaemia	24	34.8
Carotid artery stenosis	9	13
Pheripheral arteral disease	3	4.3
RCA disease	33	47.8
LMCA disease	2	2.9

MI: Myocardial infarction; PCI: Percutaneouscoronary-intervention; LMCA: Left main coronary artery; CAD: Coronary artery disease; RCA: Right coronary artery

Table 2 Peroperative data of the patients

	Patients (n)	(%)
Atrial fibrillation	10	14.4
IC Inotrope	9	13
IABP usage	1	1.44
Renal dysfunction	4	5.8
Pleural effusion	3	4.3
Prolonged airleaking	3	4.3
Mean IC stay (day)	2.83 ± 1.19	1–8
Prolonged IC stay	2	2.9
Meanhospitalstay (day)	7.65 ± 3.26	6–32
Superficial wound infection	2	2.9
Respiratory failure	2	2.9
Mean ventilation time (h)	8.14 ± 4.9	3–40
Prolonged ventilation	1	1.44
Deep wound infection	1	1.4
Sternal dehiscense	1	1.4
Pericardialeffusion	1	1.4

IABP: Intraaortic balloon pump; IC: Intensive care unit

During postoperative long term follow-up, transthoracic echocardiography was, on average, performed 31.37 ± 17.69 (9–100) months later. The long term data (≥30 days) regarding the patients are shown in **Table 3**.

During long term follow-up, newly emerging mitral valve regurgitation was observed in 23.2% (n = 16) of the patients, while newly emerging tricuspid valve regurgitation was observed in 21.7% (n = 15) of the patients. Clinical significance was not considered, since the maximum level of valve regurgitation was first degree.

Cerebrovascular events were not observed during early term follow-up. However, a cerebrovascular event was observed in one (1.4%) of the patients during long term follow-up; this event resulted in a loss of strength in the extremities.

Table 3 Long term datas (≥30 days) are presented

	Patient (n)	(%)
New developed MR	16	23.2
New developed TR	15	21.7
Plevral efüzyon	2	2.9
Pericardial effusion (minimal)	1	1.4
Late mortality	4	5.79
Atrial fibrillation	0	0
Atrial arrythmia	1	1.4
Cerebrovascular event	1	1.4

MR: Mitral regurgitation; TR: Triküspit regurgitation

Supraventricular tachyarrhythmia was observed in 1.4% (n = 1) of the patients. On the other hand, ventricular arrhythmia was not observed in any of the patients.

No increase was observed in the NYHA functional classification in 84% of the patients. A decrease in functional classification was observed in 4% of the patients, while an increase in functional classification was observed in 15% of the patients. The changes in functional classification are shown in **Fig. 1**.

The mean preoperative ejection fraction of the patients was 45.28 ± 9.67 (25–65), while the mean postoperative ejection fraction was 46.03 ± 12.4 (20–65). No significant difference was identified between these two parameters (p = 0.447).

The mean preoperative PAP was 36.67 ± 6.81 (30–60) mmHg, while the mean postoperative PAP was 37.81 ± 10.07 (20–70) mmHg. No significant difference was identified between the preoperative and postoperative values (p = 0.378).

Long term mortality was observed in 5.79% (n = 4) of the patients. During the mean follow-up period of 33.9 ± 17 (9–100) months, the mean survival rate was 94.7%.

Discussion

Pulmonary arterial hypertension is a progressive disease with a high rate of mortality that can lead to right heart failure due to increased pulmonary vascular resistance.

Left ventricle dysfunction disrupts right ventricle functions by increasing pulmonary arterial pressure, which causes biventricular dysfunction. Optimum treatment of the underlying left heart disease is recommended for patients who have PH due to left heart disease (Group I Proof C).[9] Currently, one of the most effective and

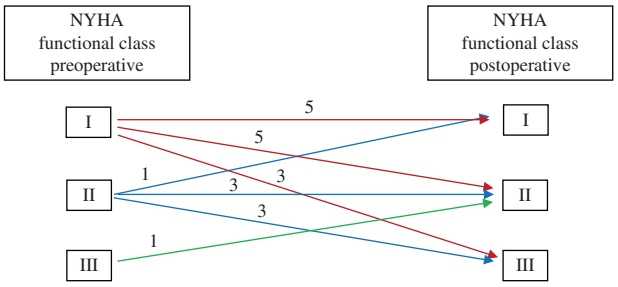

Fig. 1 The changes of functional classification in a diagrammatic image. NYHA: New York Heart Association

common methods in treatment of ischemic heart disease is coronary artery surgery.

In recent years, coronary artery surgery is commonly performed in patients who have comorbidities and high risk factors (advanced age, history of open heart surgery, widespread coronary lesion, ventricular dysfunction, poor respiratory and renal functions, need for complex/long/urgent surgical intervention).[10-12] Surgical success thus depends not only on effective surgery techniques, but also on determining risk factors preoperatively, and eliminating them by taking preventive measures if possible. Predicting risk based on a good preoperative evaluation is essential for determining the severity of the patient's condition, and for better planning the type of care that needs to be provided. The resulting improved care is associated with a better clinical condition for the patients during their intraoperative and postoperative period.[13]

Despite the advances in heart surgery, postoperative mortality and morbidity following coronary artery surgery continues to be a significant problem.[14,15] PH is another important factor that needs to be considered with regards to perioperative morbidity and mortality after coronary artery surgery. PH can alter cardiac output through its effects on the right ventricle afterload, and may also serve to indicate left ventricle dysfunction.[16]

Patients with moderate and high risk were operated in our study. The mean Euroscore was 4.49 ± 3.21 (0–14). Long term mortality was observed in 5.79% of the patients (n = 4); two of these patients experienced sudden death, while the two others died due to non-cardiac causes (non-Hodgkin's lymphoma and a pedestrian traffic accident). In addition, during the mean follow-up period of 33.9 ± 17 (9–100) months, the mean survival rate was 94.7%.

Other factors that are generally associated with early postoperative morbidity in open heart surgeries include the duration of the surgery, the duration of CPB, the duration of the aortic cross-clamp, the need for inotropic support, and the need for IABP. Different studies have illustrated the effect of the duration of cardiopulmonary bypass on morbidity and mortality.[17–19] In our study, the mean duration of cardiopulmonary bypass was 80.66 ± 22.92 (27–128) min, the mean duration of cross-clamp was 67.88 ± 19.59 (19–105) min, and the mean number of bypasses was 2.25 ± 0.83 (1–5). During the early postoperative intensive care period, 9 (13%) of the patients required inotropic support, while 1 (1.4%) of the patients required IABP.

Atrial fibrillation is a frequently observed complication that affects the survival rate and late cardiac events.[20] Atrial fibrillation was the most common complication in the early postoperative period in our study.

The increased need for inotrope during intensive care was the second most frequently observed complication, while temporary renal dysfunction was the third most frequently observed complication. We also observed a good response to medical treatment in patients with atrial fibrillation. Early stage temporary renal dysfunction was considered as systemic inflammatory response due to cardiopulmonary bypass system.

Pulmonary arterial hypertension (PAH) is a syndrome in which pulmonary vascular cross sectional area and compliance are reduced by vasoconstriction, vascular remodeling, and inflammation.[21] Moreover, following the contact between blood and artificial surfaces other than the endothelium, endothelial dysfunction occurs in the pulmonary artery bed as a result of the activation of various cascades and the release of various mediators (thrombin, free oxygen radicals, vasoactive mediators). These events can further lead to a worsening of PH, pulmonary edema, and hypoxia.[22–24] As the potential increase in resistance due to the combination of PH and of these factors can lead to a severely negative outcome, clinicians should pay attention to hemodynamic stabilization.

In light of the general mechanisms described above; methyl prednisolone, theophylline ethylenediamine, and acetylcysteine were administered before removing the cross-clamp to suppress the inflammatory cascade originating from the bypass system, as well as the potential responses. Postural drainage and lung care were provided to patients after extubation. Lung exercises were also performed.

Conclusion

In this study, we determined that the rate of PH accompanying ischemic heart disease did not show a significant

difference in the long term after surgical revascularization. We did not observe an increase in NYHA functional classification in 84% of the patients.

Given that there was no significant difference between preoperative and postoperative pulmonary arterial pressure and ejection fraction values, we believe that surgical revascularization decreases or suppresses the progression of PH, and thus contributes to quality of life of the patients.

Long term follow-up showed newly developing mitral and tricuspid valve regurgitation. Clinical significance was not considered, since the maximum level of valve regurgitation was first degree. Based on the potential of progression in valve regurgitation, periodic follow-up was recommended.

Our findings demonstrated that (1) coronary artery surgery can be safely performed in patients with PH, provided that the preoperative evaluation is good and the necessary preventive measures are taken; (2) that PH progression can be stopped by surgical revascularization; and (3) that our patients lived an average 94.7 months without any change in quality of life. Considering the low number of studies on the late stage consequences and effects in this group of patients, we believe that further prospective, randomized, controlled studies with larger patient series will be necessary.

Disclosure Statement

The authors have no conflict of interest to declare.

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