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The effects of pulmonary hypertension on early outcomes in patients undergoing coronary artery bypass surgery

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Background/aim: To investigate the effects of pulmonary hypertension on early clinical variables in patients undergoing coronary artery bypass grafting surgery.

Materials and methods: The preoperative echocardiographic data of patients who underwent isolated coronary artery bypass surgery were evaluated retrospectively. A total of 1244 patients were included in the study. The patients were divided into two groups: one group consisted of patients with systolic pulmonary artery pressure (SPAP) values equal to or greater than 30 mmHg (Group 1, n = 184), while the other group consisted of patients with SPAP values below 30 mmHg (Group 2, n = 1060).

Results: Early mortality was similar in both groups (0% in Group 1 and 1.2% in Group 2; $P > 0.05$). Comparison of postoperative data indicated that Group 1 had a higher need for inotropic agent treatment, a longer average duration of ventilation, and a longer average duration of stay in the intensive care unit ($P < 0.05$). For the other variables, no significant differences were identified between patients with and without pulmonary hypertension ($P > 0.05$).

Conclusion: Mild pulmonary hypertension (mean SPAP = 37.7 ± 8.4 mmHg) was not associated with a significant difference in the mortality of patients undergoing coronary artery bypass grafting. For patients undergoing this type of coronary bypass surgery, lower morbidity and mortality rates can be achieved through comprehensive preoperative examinations and effective perioperative medical procedures.

Key words: Coronary artery bypass, pulmonary hypertension, mortality, morbidity

1. Introduction

Pulmonary hypertension (PH) is a hemodynamic and physiopathological condition that can be caused by a large variety of clinical conditions such as collagen tissue diseases, left atrial or ventricular cardiac diseases, diseases of the left heart valve, chronic thromboembolism, and interstitial pulmonary diseases (1).

Increase in pulmonary vascular resistance leads to PH, the most severe and potentially detrimental chronic disorder of pulmonary circulation. Due to its variable etiology and pathogenesis, diagnosis and treatment of this hemodynamic disorder is challenging for physicians (2).

In patients with acquired cardiac disease, PH is most often due to elevated left atrial pressure (3). PH is defined as mean pulmonary artery pressure (PAP) of ≥25 mmHg at rest as evaluated by right cardiac catheterization (RCC) (4). PH is also defined as mean PAP of >30 mmHg during exercise (as evaluated by RCC), but this definition is not supported by the existing literature (5,6).

PH is a known risk factor for morbidity and mortality among patients undergoing coronary artery bypass grafting (CABG) surgery. However, the limited literature on this topic is somewhat inconsistent and reveals many unanswered questions (7). Intraoperative and postoperative risk management is crucial for these patients. There are only a limited number of studies investigating outcomes for this patient group.

The PH of patients can be easily examined using cardiac catheterization and echocardiography. Such examinations provide insight regarding potential intraoperative and postoperative risks and are also important for taking preventive measures against possible complications. In the present study, we evaluated the effect of PH on the early-stage outcomes in patients who underwent CABG.

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2. Materials and methods

This study was performed by retrospective evaluation of the preoperative echocardiographic data of patients who underwent isolated coronary artery bypass graft surgery between March 2003 and March 2012.

A total of 1244 patients were included in the study. Patients with comorbidities that would lead to increased pulmonary artery pressure, patients with primary PH, and patients who underwent additional surgeries such as aortic surgery, aneurysmectomy, and heart valve intervention were excluded from the study. The patients were divided into two groups: one group consisted of patients with systolic pulmonary artery pressure (SPAP) values equal to or greater than 30 mmHg (Group 1, n = 184), while the other group consisted of patients with SPAP values below 30 mmHg (Group 2, n = 1060). The mean pulmonary artery pressure in Group 1 was 37.7 ± 8.4 mmHg (range: 30–75).

SPAP was calculated based on tricuspid regurgitation by using the modified Bernoulli equation and by exercising maximum caution in transthoracic echocardiography. To this end, we selected the tricuspid regurgitation best viewed under color Doppler echocardiography, and the acoustic window with an angle between the ultrasound beam and the direction of flow that was as close as possible to 0°. In addition, we took into account the tricuspid regurgitation jet that was the densest and that had an apparent selected peak in the continuous wave Doppler.

2.1. Anesthesia

Patients were monitored after being transferred to the operation room. A pulse oximetry probe was attached in order to monitor peripheral arterial oxygen saturation. A 20 G cannula was placed in the right radial artery to monitor the systemic arterial pressure and arterial blood gas. Anesthesia was induced with a mixture of 2% lidocaine (1 mg/kg), midazolam (0.2–0.3 mg/kg), fentanyl (5 µg/kg), and vecuronium (0.1 mg/kg). All patients were manually respirated, intubated following complete muscle relaxation, and connected to a mechanical ventilator. Anesthesia was maintained with fentanyl (10–30 µg/kg) and midazolam (0.1–0.3 mg kg^{-1} h^{-1}). Prior to the surgical incision, 1 g of cefazolin sodium was administered intravenously for antibiotic prophylaxis.

2.2. Surgical technique

All operations were performed by using a median sternotomy under cardiopulmonary bypass (CPB). A roller pump, nonheparin-coated oxygenator, polyvinylchloride tubing set, and two-step venous cannula were used for the CPB. Mild systemic hypothermia (33–34 °C) and a nonpulsatile pump flow (2.4 L min^{-1} m^{-2}) were used. Throughout CPB, hematocrit was maintained between 22% and 25%, while mean arterial pressure was maintained between 50 and 70 mmHg. Anticoagulation was provided with heparin to ensure an active coagulation time of >480 s just before the CPB. Antegrade and retrograde blood cardioplegia were used for myocardial protection. Warm blood cardioplegia was administered before removing the aortic cross-clamp. The internal mammary artery (IMA) was preferred for LAD artery anastomosis in all patients; however, a saphenous venous graft was used in cases where an IMA graft was not suitable. In suitable cases with multiple coronary artery disease, radial artery and/or saphenous venous grafts were chosen in addition to the IMA graft. Distal anastomoses were performed under cross-clamp with 7-8/0 prolene suture, while proximal anastomoses were performed under cross-clamp with 6/0 prolene suture. Prior to the removal of the cross-clamp, pulmonary hypertensive patients were administered with methylprednisolone, theophylline ethylenediamine, and acetyl cysteine. During postoperative intensive care, pulmonary hypertensive patients were administered with intravenous nitroglycerine infusions and with acetyl cysteine (administered intravenously during intensive care and orally afterwards). Prior to extubation, methylprednisolone, theophylline ethylenediamine, acetyl cysteine, and lidocaine were administered to pulmonary hypertensive patients who were scheduled for extubation. Lung care was provided with postural drainage in all extubated patients. Bronchodilator treatment with a nebulizer and vapor treatment were also performed when necessary.

2.3. Statistical analysis

SPSS for Windows 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. For continuous variables, the fitness to normal distribution and homogeneity were tested using the Kolmogorov–Smirnov test and the Levene test, and the data were classified accordingly. Categorical data were analyzed by using the chi-square test or Fisher exact test. The independent samples t-test was used for parametric variables. The values were presented as mean ± standard deviation (SD). $P < 0.05$ was considered statistically significant.

3. Results

An evaluation of the patients' demographic features indicated that the PH group included a higher number of patients with low ejection fraction (EF) and advanced age, as well as a higher number of female patients ($P < 0.05$). In addition, the PH group had significantly more patients with second-degree mitral failure (MF), high Euroscores, a history of comorbid chronic obstructive pulmonary disease (COPD), and a history of preoperative myocardial infarction (MI) ($P < 0.05$). Early mortality (≤30 days) was not observed in the PH group. The rate of early mortality was similar in both groups (0% in Group 1 and 1.2% in Group 2; $P > 0.05$). The distribution of demographic features of groups are presented in Table 1.

Table 1. Demographical data and their distribution with respect to the groups.

	Group 1 (n = 184)	Group 2 (n = 1060)	P-value
Emergency operation, %	1.6	3.4	0.205
EF, mean ± SD	44.8 ± 10.2	50.19 ± 9.2	0.042
Family history, %	34.8	31.2	0.339
Second-degree history, %	26.6	10.3	0.0001
Age years, mean ± SD	64.8 ± 9.2	60.5 ± 9.7	0.0001
Sex (female), %	35.9	23.8	0.001
Euroscore, mean ± SD	5.13 ± 2.56	3.8 ± 2.44	0.0001
Unstable angina, %	21.2	17.4	0.210
Diabetes mellitus, %	25	24.2	0.826
Hypertension, %	39.7	34.5	0.178
Obesity, %	20.1	19.5	0.855
BMI, mean ± SD	26.25 ± 4.2	26.8 ± 7.62	0.36
COPD, %	20.7	13.2	0.008
Pre-MI, %	67.4	58.2	0.019
Renal failure, %	3.3	2.3	0.416
Hyperlipidemia, %	32.4	38.8	0.387
PTCA, %	9.2	10.5	0.64
Previous CVE, %	1.6	2.2	0.637

BMI: Body mass index, EF: ejection fraction, COPD: chronic obstructive pulmonary disease, Pre-MI: preoperative myocardial infarction, PTCA: percutaneous transluminal coronary angioplasty, CVE: cerebrovascular event.

Between the groups, there were no significant differences in the number of bypass operations, left IMA use, cardiopulmonary bypass time, and cross-clamp time. Operative data and their distributions with respect to the groups are presented in Table 2.

Comparison of postoperative findings indicated that the rate of early mortality was similar in both groups (0% in Group 1 and 1.2% in Group 2; $P > 0.05$). The mean ventilation time and the mean duration of stay at the intensive care unit were longer in Group 1.

Furthermore, there was an increased need for inotropic agent treatment in Group 1 ($P < 0.05$). Between the two groups, there were no significant differences in the hospitalization time and other parameters ($P > 0.05$). Postoperative data and their distribution with respect to the groups are presented in Table 3. Sternal dehiscence and reexploration were not observed in the PH group.

4. Discussion

Despite advances in cardiac surgery, morbidity and mortality after coronary heart surgeries still continue to represent a major medical problem in our day (8). PH is an important factor with respect to perioperative mortality and morbidity in coronary bypass surgery, and since PH affects the right ventricle afterload, it can cause changes in the cardiac output or indicate left ventricle dysfunction (9). There is a surprising paucity of information in the recent literature regarding the impact of PH in cardiac surgery, as most studies appear to focus on valve diseases (10–13).

In open cardiac surgeries, operation time, CPB time, aortic cross-clamp time, the need for inotropic support, and the need for intraaortic balloon pump are variables that can be correlated with early postoperative morbidity and mortality.

Table 2. Operative data in both groups.

	Group 1 (n = 184)	Group 2 (n = 1060)	P-value
Number of bypasses, mean ± SD	2.46 ± 0.89	2.56 ± 0.89	0.128
LIMA, %	95.1	97.3	0.117
Pump time, mean ± SD	83.8 ± 20.48	83.03 ± 22.56	0.787
XL time, mean ± SD	69.21 ± 17.69	69.76 ± 18.34	0.756
Age years, mean ± SD	64.8 ± 9.2	60.5 ± 9.7	0.0001

LIMA: Left internal mammary artery, XL: cross-clamp.

Table 3. Postoperative data in both groups.

	Group 1 (n = 184)	Group 2 (n = 1060)	P-value
Prolonged ventilation, %	2.2	0.7	0.006
Prolonged IC stay, %	5.4	2.6	0.042
AF, %	15.8	12.5	0.292
IC inotrope, %	13	5.7	0.0001
IABP usage, %	1.6	0.8	0.317
VT, mean ± SD	8.81 ± 5.9	7.51 ± 4.25	0.002
IC stay days, mean ± SD	2.69 ± 1.27	2.47 ± 1.12	0.09
Hospital stay days, mean ± SD	7.07 ± 2.22	6.88 ± 1.96	0.243
Mortality, %	0	1.2	0.13
Sternal dehiscence, %	0	0.8	0.237
Reexploration, %	0	1.4	0.104

AF: Atrial fibrillation, VT: ventilation time, IC: intensive care, IABP: intraaortic balloon pump.

Kennedy et al. previously reported that in patients with isolated CABG, an increase in mean pulmonary arterial pressure was associated with an increase in mortality rates (with normal, mild, moderate, and severe pulmonary arterial pressure leading to mortality rates of 0.9%, 1.7%, 8.1%, and 21.6%, respectively; $P < 0.001$). Kennedy et al. also noted in their study that morbidity and mortality were independently associated with PH. For patients with moderate and severe PH, and particularly in cases of isolated CABG, Kennedy et al. observed that mortality rates were significantly higher than the rates predicted by the STS model (7). In the present study, no mortality was observed in Group 1, while the rate of mortality in Group 2 was 1.2%. There was no significant difference in the mortality rates of the groups.

In the present study, we mainly examined the effect of PH on early-stage outcomes after coronary bypass surgery. In addition, the findings of our study were also evaluated with respect to the parameters that impact this surgery, including surgery time, CPB time, aortic cross-clamp time, mechanical ventilation time, and need for inotropic and mechanical support.

The activation of inflammatory cascades and the release of mediators (thrombin, free oxygen radicals, vasoactive mediators) due to the CPB system leads to endothelial dysfunction in the pulmonary vascular bed, which can further trigger hypertension, pulmonary edema, and hypoxia in the pulmonary circulation (14,15). Together with these disorders, PH can lead to increased resistance and severe hemodynamic disturbances. Aortic cross-clamp time and surgery time are correlated with the duration of CPB and can be associated with the abovementioned negative effects. The absence of significant differences in operative parameters between the groups was important in allowing the identification of PH-related effects; we think that this further ensured the reliability of the study results.

PH without any identifiable cause other than ischemic heart disease can be indicative of poor prognosis when it is present with one or more of the previously mentioned factors, which are all indicators of ischemia-related myocardial dysfunction. In this context, it is expected that PH will also affect the mechanical ventilation time, the duration of stay in the intensive care unit, and the hospital mortality rate (16).

As expected, we observed longer ventilation time, longer stay in the intensive care unit, and increased need for inotropic agents in the PH group. However, it should be noted that this group consisted of patients with high Euroscores, advanced age, and low EF. A comparison of the two study groups revealed no significant differences in left IMA use, cardiopulmonary bypass time, and cross-clamp time.

In recent years, there has been a rapid increase in the availability and number of agents for the treatment of both acute and chronic PH. While numerous studies in the literature support the use of these agents for treating primary pulmonary arterial hypertension, there is less information concerning their use in the treatment of left-sided heart diseases. Although epoprostenol, nitric oxide, sildenafil, and milrinone are commonly employed for the perioperative management of cardiac surgery patients, studies describing their use have been limited in number and have focused mainly on hemodynamic end points rather than clinical ones (10,17–19). As described in greater detail in Section 2, the preoperative treatment administered in our study was based on the use of intravenous nitroglycerin.

The limitations of our study included the fact that it was a retrospective, single-center study, and the fact that pulmonary artery pressure was measured by transthoracic echocardiography instead of right heart catheterization. Another limitation of the study was the low number of patients in the PH group. To better demonstrate the effects of PH, the current study needs to be further supported by prospective and randomized studies.

In conclusion, while we did not observe a significant difference in mortality rates between CABG patients with mild PH (mean SPAP = 37.7 ± 8.4 mmHg) and CABG patients with normal pulmonary artery pressure, the PH group exhibited longer ventilation time, longer stay in the intensive care unit, increased need for inotropic agents, and more potentially problematic patients.

It is possible to ensure low mortality and morbidity rates in coronary bypass surgeries by carefully examining these patients during the preoperative period, and by choosing the appropriate intraoperative and postoperative medical approaches.

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