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Effect of Postoperative Constrictive Physiology on Early Outcomes after Off-Pump Coronary Artery Bypass Grafting

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Background: Constrictive pericarditis after coronary artery bypass surgery has been known to affect cardiac output by limiting diastolic ventricular filling. We aimed to assess the influence of postoperative constrictive physiology on the early outcomes of patients undergoing off-pump coronary artery bypass grafting (OPCAB). ***Materials and Methods:*** Between January 2008 and July 2011, 903 patients underwent an isolated OPCAB and postoperative transthoracic-echocardiography. The patient cohort was classified into two groups: group A, constrictive physiology and group B, control group without constrictive physiology. Early outcomes were analyzed between the two groups. ***Results:*** Of the total 903 patients, group A consisted of 153 patients (16.9%). The amount of blood loss in group A during the postoperative 24 hours was greater than that of group B, but this was not statistically significant (p=0.20). No significant differences were found in the mortality rates (group A, 0.6%; group B, 1.4%; p=0.40) and 30-day major adverse cardiac and cerebrovascular events (MACCEs; group A, 3.3%; group B, 6.1%; p=0.42). ***Conclusion:*** Postoperative constrictive physiology does not affect 30-day MACCEs or other major complications after OPCAB. The results of this study suggest that patients with early postoperative constrictive physiology do not need medical or surgical treatment, and that conservative care is sufficient.

Key words: 1. Constrictive pericarditis
2. Coronary artery bypass, off-pump

INTRODUCTION

Constrictive pericarditis is a progressive condition that is characterized by pericardial fibrosis with or without calcification, and impairs ventricular filling. This leads to venous congestion and diminished cardiac output [1]. The most common cause of constrictive pericarditis is previous cardiac surgery, followed by thoracic radiation, previous myocardial infarction, idiopathic disease, and infection [2]. In the past, the development of constrictive pericarditis was believed to be irreversible, but recent studies have reported the resolution of a transient form of constrictive pericarditis without surgical intervention [3,4]. Moreover, approximately 60% of patients with constrictive pericarditis caused by cardiac surgery have been shown to have constrictive physiology on postoperative echocardiography [3].

The prognosis and natural history of constrictive physiology after pericardiotomy is unclear. Therefore, we aimed to assess whether constrictive physiology based on early postoperative echocardiography after off-pump coronary artery bypass graft (OPCAB) may require medical or surgical treatment to prevent constrictive pericarditis and whether it would have an effect on

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early mortality and morbidity of patients undergoing OPCAB.

MATERIALS AND METHODS

1) Study population

Between January 2008 and July 2011, 903 patients underwent isolated OPCAB at Yonsei Cardiovascular Hospital and were enrolled in this single center, randomized, retrospective study. All of the patients received tissue Doppler transthoracic echocardiography at postoperative day 7. The 903 patients were divided into two groups. Group A consisted of patients who showed constrictive physiology on postoperative echocardiography, and group B was the control group that consisted of the patients without evidence of constrictive physiology. Mortality, 30-day major adverse cardiac and cerebrovascular events (MACCEs), surgical characteristics, and other complications were compared between the two groups. Two patients who showed acute constrictive pericarditis were excluded from the study.

2) Surgical technique and postoperative management

All the patients underwent surgical bypass using the off-pump method and median sternotomy. Systemic heparinization was administered to maintain an activated clotting time of 250 seconds during the operation. A commercially available cardiac stabilizer and an apex vacuum device were used for cardiac displacement and stabilization. The internal mammary artery (IMA) was harvested using a semi-skeletonized technique. In most cases, the left IMA was anastomosed to the left anterior descending artery. For the other left coronary artery regions, a radial artery or saphenous vein graft was used as a composite graft. For right coronary artery bypass, the radial artery or a saphenous vein free graft attached to the left IMA was used in the majority of the cases depending on the degree of native coronary artery stenosis and the degree of aortic atherosclerosis. Postoperative dual antiplatelet therapy was maintained for at least 9 months unless contraindicated. Statins were routinely used during the study period, and a small dose of diuretics was administrated until the patients were discharge according to their conditions.

3) Follow-up, data collection, and definitions

All of the patients' charts were reviewed, and data were collected retrospectively from the reviewed charts. The patients' preoperative baseline characteristics, surgical record, postoperative complications including 30-day MACCEs, renal failure, respiratory complications, early postoperative echocardiography, intensive care unit (ICU) stay, and hospital stay were reviewed. Constrictive physiology was defined as septal bouncing and flattening of the left ventricular posterior wall during diastole, respiratory variation in ventricular size (inferior vena cava plethora), respiratory variation of 25% or more in the mitral inflow E velocity, increased diastolic flow reversal with expiration in the hepatic vein, E' $\geq$7-8 cm/sec with respiratory variation of E', and absence of pericardial thickness and calcification. A MACCE was defined as the occurrence of death by any cause, nonfatal myocardial infarction, a stroke, or the need for target vessel revascularization. Myocardial infarction was defined as creatine kinase muscle-brain elevation with the appearance of a new Q-wave or S-T segment elevation greater than 2 mm on an electrocardiogram. The diabetic patients were defined as patients receiving an oral hypoglycemic agent or insulin. The chronic renal failure patients were defined as those who required hemodialysis, peritoneal dialysis, or whose preoperative serum creatinine level exceeded 2.0 mg/dL. The primary endpoint of the study was cardiac death and MACCEs.

4) Statistical analysis

Statistical analyses were performed using statistical software SPSS ver. 13.0 (SPSS Inc., Chicago, IL, USA). The values for continuous variables were displayed as mean±standard deviation. For the comparison of two variables, the Student's t-test and χ^2 test were used. Statistical significance was defined as a p-value less than 0.05.

RESULTS

1) Patient characteristics

Among the 903 patients included in this study, 153 (17%) were diagnosed with constrictive physiology (group A). None of these patient displayed typical symptoms of pericarditis. They were not given specific treatment for constrictive physiology, and 1-year follow-up echocardiography showed complete resolution of the constrictive physiology in all 153

Table 1. Baseline demographics and clinical characteristics

Characteristic	Group A (n=153, 17%)	Group B (n=750, 83%)	p-value
Age (yr)	65.3±9.3	65.4±8.6	0.91
Women	33 (22)	220 (30)	0.04
Body mass index (kg/m^2)	24.6±9.3	24.5±3.7	0.76
Hypertension	97 (63)	544 (73)	0.03
Diabetes mellitus	59 (39)	336 (45)	0.15
Current smoker	38 (25)	157 (21)	0.31
PAOD	21 (14)	75 (10)	0.21
Cerebrovascular accident	24 (16)	85 (11)	0.17
Dyslipidemia	55 (36)	289 (39)	0.52
Chronic renal failure	19 (12)	103 (14)	0.66
Ejection fraction (<35%)	10 (7)	92 (12)	0.05
EuroSCORE	3.81	4.03	0.30
EuroSCORE (>5)	30 (22)	199 (27)	0.50
NYHA class	1.78±0.6	1.85±0.6	0.30
Coronary artery disease no	2.81±0.5	2.79±0.5	0.61

Values are presented as mean±standard deviation or number (%). PAOD, peripheral artery occlusive disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New York Heart Association.

patients. The baseline demographics and preoperative clinical characteristics are shown in Table 1. Group A showed a low representation of women (p=0.04), a low incidence of hypertension (p=0.03), and low ejection fraction (p=0.05) compared to group B. Other reviewed data showed no significant differences between the two groups.

2) Operative and postoperative results

There were no significant differences between the two groups in the number of distal anastomosis and in the operative time (Table 2). Increased blood loss and transfusion volumes during the first postoperative 24 hours were observed in group A compared to group B, but these differences were not statistically significant (p=0.20). Other postoperative comparisons such as hospital stay and ICU stay showed no significant differences between the two groups (Table 3).

3) Early mortality and major adverse cardiac and cerebrovascular events

Thirty-day MACCEs including death by any cause, nonfatal myocardial infarction, and stroke were not significantly different between the two groups. There were also no significant differences in respiratory complications (such as pneumonia, prolonged ventilator care, or acute respiratory distress syndrome) and renal failure (such as the need for renal replacement treatment). Admissions for more than 12 days and prolonged hospitalizations were also not significantly different between the two groups.

Table 2. Operative and postoperative data

	Group A	Group B	p-value
Anastomosis per patient	3.21±0.8	3.18±0.9	0.74
Operative time (min)	241.0±44.6	239.3±44.5	0.69
Blood loss[a] (mL)	834.7	789.8	0.20
Transfusion amount[a] (mL)	267.7	162	0.93
ESR[b]	53.1±25.5	54.2±26.4	0.65
CRP[b]	44.7±42.5	44.9±41.2	0.96
ICU stays (hr)	66.43±5.6	62.54±5.9	0.37
Hospital stay (day)	11.9±11.1	13.5±13.8	0.52

Values are presented as mean±standard deviation or number (%). ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ICU, intensive care unit.
[a]During postoperative 24 hours.
[b]At postoperative 7th day.

Table 3. Adverse events after surgery

	Group A	Group B	p-value
Thirty-day MACCEs			
Mortality	1 (0.6)	11 (1.5)	0.41
Perioperative MI	5 (3.3)	46 (6.1)	0.27
Stroke	2 (1.3)	5 (0.7)	0.97
Renal failure	14 (9.2)	70 (9.3)	0.82
Respiratory complications	5 (3.3)	37 (4.9)	0.86
Prolonged hospitalization[a]	53 (34)	225 (30)	0.31

Values are presented as number (%).
MACCEs, major adverse cardiac and cerebrovascular event; MI, myocardial infarction.
[a]Over 12 days.

DISCUSSION

Constrictive pericarditis, a compressed ventricle, and impaired ventricular filling have been shown to occur because of tuberculosis, uremia, previous thoracic irradiation, and past chest trauma; however, recently the most common cause of

constrictive pericarditis has been shown to be previous cardiac surgery [1,2]. Pericardiotomy with concurrent cardiac surgery leads to a transiently thickened and inelastic pericardium, resulting from edema, fibrin deposition, or inflammation. Moderate amounts of pericardial effusion then develop without evidence of constriction. Approximately 1 to 2 weeks later, constrictive physiology develops. In the last phase, pericardial effusion resolves or decreases in size, and the hemodynamics normalize with no evidence of constriction recurrence in most patients. However, in some patients, pericardial inflammation continues and pericardial fibrosis and calcification subsequently develop, leading to chronic constrictive pericarditis [3-5].

The common symptoms of constrictive pericarditis have been dyspnea on exertion, chest pain, fever and a sign of right heart failure consistent with edema, abdominal swelling, and jugular venous distension [3,6]. As mentioned above, a transient form of constrictive pericarditis can be resolved with medical treatments including a nonsteroidal anti-inflammatory drug (NSAID), steroids, and diuretics without surgical intervention [3]. However, refractory chronic constrictive pericarditis often needs pericardiectomy.

Approximately 60% of the patients with constrictive pericarditis caused by cardiac surgery have shown constrictive physiology on postoperative echocardiography [3]. Specifically, constrictive pericarditis after coronary artery bypass graft (CABG) has been reported in a few studies where symptoms developed from myocardial ischemia because of graft occlusion derived from diastolic dysfunction of constrictive pericarditis. These cases had required repeat CABG including extensive decortication of the left ventricle, right atrium, and right ventricle [7,8]. Constrictive pericarditis following coronary bypass surgery is an unusual complication with an occurrence rate of 0.2% to 0.3% [9], but as mentioned earlier, serious negative results can develop.

In the same way, postoperative constrictive pericarditis can have an unfavorable effect on the prognosis of patients undergoing cardiac surgery, especially CABG. However, the prognosis and natural history of constrictive physiology after pericardiotomy is unclear. Therefore, we analyzed whether constrictive physiology seen on early postoperative echocardiography after OPCAB may require treatment to prevent constrictive pericarditis and whether it would have an effect on early mortality and morbidity of patients undergoing OPCAB.

In our study, constrictive physiology on postoperative echocardiography was observed in 153 (17%) patients with isolated OPCAB. No patient displayed any typical symptoms of pericarditis, and no patient received preventive medication or specific treatments for constrictive pericarditis. After 1 year, follow-up echocardiography showed complete resolution of constrictive physiology in all the patients. There were no significant differences in the postoperative mortality and morbidity rates between the two groups. Therefore, we suggest that if a patient showing constrictive physiology on early postoperative echocardiography is hemodynamically stable and has no symptoms, specific medication is not needed and a follow-up echocardiography should be considered.

Transient constrictive pericarditis was originally described in the English literature by Sagrista-Sauleda et al. [4] in 1987. They reported the development of objective evidence for constrictive physiology occurring in 16 of 177 patients (9%) with effusive acute idiopathic pericarditis, which subsequently resolved with conservative treatment. The interval of time until the first echocardiogram showing pericardial effusion ranged from 5 to 30 days. The time to normalization of the noninvasive recordings for all the patients ranged from 7 days to 58 months. At a mean follow-up of 31 months, none of the patients had presented with a recurrence of constriction. The authors suggested that the mechanism responsible for the findings in these patients was a transiently thickened and inelastic pericardium resulting from edema, fibrin deposition, or inflammation. Similarly, we thought that constrictive physiology does not accompany pericardial fibrosis, calcification rarely progresses to constrictive pericarditis, and resolution occurs with conservative treatment.

In the cases of constrictive physiology followed by pericardiotomy, pericardial effusion plays a major role in the pathophysiology. Therefore, we assumed that postoperative bleeding, tube drainage volumes, and ICU stay duration that disturb ambulation are risk factors for constrictive physiology. In our study, group A had more blood loss and a longer ICU stay, but these were not statistically significant. Therefore, we were unable to identify the risk factors for constrictive pericarditis. Matsuyama et al. [6] reported the clinical characteristics of 11 patients that developed postoperative con-

strictive pericarditis among a total of 463 CABG patients. Ten patients (91%) had evidence of pericardial effusion, which was the primary risk factor for postoperative constrictive pericarditis. In addition, left ventricular ejection fraction and warfarin administration were risk factors for postoperative constrictive pericarditis based on multivariate analysis. Effler [10] reported that residual blood elements within the pericardial sac, especially in the areas of major involvement, were found at the time of cardiac surgery in most of the patients with chronic constrictive pericarditis of various etiologies. Cohen and Greenberg [11] also explained that organized hematomas, loculated clots, and unclotted viscous blood within the pericardial space were the most important causes of constrictive pericarditis after cardiac surgery.

Most of the studies until now, and those cited above, are studies of on-pump CABG, and a study on constrictive pericarditis after OPCAB can only be found in one case report [12]. Elena [13] reported that a prolonged cardiopulmonary bypass time is an independent risk factor for pericardial effusion after cardiac surgery because of the systemic inflammatory response. Although no study has compared on-pump CABG with OPCAB, the on-pump CABG can be a risk factor for constrictive pericarditis compared with OPCAB because on-pump CABG has a risk for pericardial effusion caused by a systemic inflammatory response.

The main limitation of this study is the retrospective design. Pericardial effusion is the most important factor in constrictive physiology, but we were unable to find the appropriate factors that represent the effectiveness and factors disturbing tube drainage that affect pericardial effusion. Because our follow-up duration was limited to the immediate postoperative period, the clinical symptoms were mixed, with postoperative chest pain, fever, and other symptoms. Therefore, we cannot evaluate the clinical symptoms of constrictive physiology. Lastly, because our follow-up period was short, a study with a long term follow-up period and repeated echocardiographic data is necessary to confirm our conclusions.

CONCLUSION

Postoperative constrictive physiology does not affect 30-day MACCEs or other complications after OPCAB. The results of this study suggest that patients with early postoperative constrictive physiology do not need medical or surgical treatment, and that conservative care is sufficient.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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