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Original Research Article

Effect of competitive flow and diltiazem on postoperative hemodynamics and long-term patency rate after coronary artery bypass grafting

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Abstract

Purpose: *To determine the effect of competitive flow and diltiazem on postoperative hemodynamics and long-term patency rate in patients undergoing coronary artery bypass grafting (CABG).*
Methods: *A retrospective analysis was performed on the clinical records of 98 patients who underwent CABG at Qilu Hospital of Shandong University from March 2018 to September 2020. Among them, 47 patients who underwent CABG alone were assigned to control group, while 51 patients who received additional diltiazem were assigned to study group. The severity of coronary artery stenosis (CAS) was evaluated through preoperative coronary angiography, and bridge vessel flow compared between severe stenosis and non-severe stenosis groups. Changes in hemodynamic parameters between two groups were compared before surgery, as well as 12 and 24 h after surgery.*
Results: *A significantly higher bridge vessel blood flow was found in severe stenosis group compared to non-severe stenosis group ($p < 0.05$). The CAS severity and bridge vessel blood flow revealed an inverse relationship ($r = -0.792$, $p < 0.001$). At 12 and 24 h post-surgery, the study group exhibited significantly lower central venous pressure (CVP), heart rate (HR) and mean arterial pressure (MAP) than the control group ($p < 0.05$). There was no significant difference in adverse cardiovascular effects (ACEs), between the two groups after 12 months ($p > 0.05$). Similarly, there was no significant difference in graft patency rate, mild stenosis rate, severe stenosis rate, complete occlusion rate, and linear signs rate 12 months post-operation ($p > 0.05$). However, the patency rate was significantly higher in cases with severe stenosis ($p < 0.05$).*
Conclusion: *Postoperative administration of diltiazem in patients undergoing CABG improves systemic hemodynamic parameters. However, competitive blood flow may potentially decrease the long-term patency rate of bridge vessels in patients.*

Keywords: *Competitive blood flow, Diltiazem, Coronary artery bypass grafting, Hemodynamics, Long-term patency rate*

INTRODUCTION

Coronary heart disease (CHD) has significantly high rates of both incidence and mortality. In China, over 10 million people have experienced CHD [1]. It is projected that by the year 2020, global death toll from CHD will reach 11.1 million people [2]. Coronary artery bypass grafting

(CABG), as a crucial method against CHD, contributes to lowering mortality and occlusion rates [3]. In CABG, the left internal mammary artery is typically preferred as the bridging vessel. However, in clinical practice, some bridge vessels may experience stenosis and occlusion soon after operation, and some patients are at an increased risk of adverse cardiovascular effects (ACEs) following the procedure [4,5]. Competitive blood flow in partially occluded coronary arteries leads to changes in flow volume and patterns in the left internal mammary artery (LIMA). This phenomenon is considered a major contributing factor to occlusion and deterioration of the LIMA graft [6]. Diltiazem is one of the most commonly used medications in clinical practice for the prevention and therapy of cardiovascular conditions, including myocardial ischemia and angina [7]. Diltiazem effectively inhibits arterial spasms after CABG surgery, thereby reducing the incidence of adverse effects, and significantly improving prognosis [8]. Nevertheless, the effect of diltiazem on hemodynamics is not fully understood, and the influence of coronary artery competitive flow on bridge vessels requires further investigation. Hence, this retrospective study was undertaken to investigate the effect of diltiazem administration on postoperative hemodynamics in patients undergoing CABG, and to identify effective methods for the prevention and treatment of early graft occlusion.

METHODS

Subjects

The medical records of 98 patients who underwent CABG in Qilu Hospital of Shandong University, Jinan, China between March 2018 and September 2020 were collected and retrospectively analyzed. Among them, 47 patients who received CABG alone were assigned to the control group while another 51 patients who received additional diltiazem as study group.

Ethical approval

This study was performed after approval from the Ethics Committee of Qilu Hospital of Shandong University (approval no. 20180122), and it complied with the guidelines of the Declaration of Helsinki [9].

Inclusion criteria

Patients with preoperative coronary angiography showing lesions in the left anterior descending branch or multiple coronary arteries, surgical indications, able to communicate normally, have clear consciousness, and detailed clinical records.

Exclusion criteria

Patients with sinus bradycardia (heart rate (HR) < 50 beats/min), grade II atrioventricular conduction block or above, obstruction of main left coronary artery ≥ 50 %, comorbid with valvular heart disease, level II hypertension or above, severe hypotension or cardiogenic shock before the operation, patients who have undergone other cardiac surgery, known allergy to drugs adopted in this study, and poor treatment compliance.

Treatments

Control group comprised patients who underwent revascularization of left anterior descending coronary artery using the left internal mammary artery as the bridge material. If the left internal thoracic artery was not suitable for use, venous bridge material would be adopted. The circumflex branch of the left coronary artery and the right coronary artery were also used as venous bridge materials. Autologous great saphenous vein was selected as the venous bridge material. Vessels were obtained according to the standard acquisition procedures for great saphenous vein bridge. End-to-end and end-to-side anastomoses were performed at target vessel ends after completion of the revascularization of bridge vessels. During operation, a real-time blood flow meter was used to ensure patency of bridge vessels, and the flow rate of bridge vessels was recorded. Antiplatelet therapy was initiated within 48 h post-operation. Study group received additional intravenous administration of diltiazem (1.0 - 5.0 μg/kg/min) through pump from the beginning of operation till 48 h after operation.

Hemodynamic parameters

Changes in hemodynamic parameters such as central venous pressure (CVP), heart rate (HR), as well as mean arterial pressure (MAP), were measured using a multi-parameter ECG monitor (Shenzhen Mindray Biomedical Electronics Co. Ltd, model I MEC6) before operation, 12 and 24 h after operation.

Evaluation criteria for severity of coronary artery stenosis (CAS)

Before operation, CAS severity assessed by coronary arteriography was calculated using the Gensini scoring system (≥ 99 % stenosis: 32 points; 90 % ≤ stenosis < 99 %: 16 points; 75 %

≤ stenosis < 90 %: 8 points; 50 % ≤ stenosis < 75 %: 4 points; 25 % ≤ stenosis < 50 %: 2 points; < 25 % stenosis: 1 point) [10]. In addition, the following coefficients were used to calculate Gensini score based on the segment of coronary artery involvement. Posterior lateral branch, second diagonal branch (coefficient of 0.5); right coronary artery, posterior descending branch, left circumflex artery, distal segment, posterior descending branch, left anterior descending artery, distal segment, and first diagonal branch (coefficient of 1); mid-segment (coefficient of 1.5); proximal segment (coefficient of 2.5); left main artery (coefficient of 5). The final Gensini score was obtained by summing up the scores of each branch, and a higher score indicates more serious coronary artery disease (CAD). Based on the final Gensini score, patients were assigned to a severe stenosis group (≥ 60, n = 37) or non-severe stenosis group (< 60, n = 61).

Postoperative follow-up evaluation

Follow-up was done for one year after operation. Coronary computed tomography angiography and color doppler echocardiography were performed to assess the patency of bridge vessels after one year of surgery. Evaluation criteria for patency were based on the degree of arterial stenosis, which was classified as follows; less than 30 % stenosis was considered patent, 30 - 49 % was classified as mild stenosis, 50 - 69 % as moderate stenosis, 70 - 89 % as severe stenosis, and 90 - 100 % as complete occlusion. Poor opacification or thinning of the graft vessel was considered a linear sign. Besides, the incidence of ACEs (angina pectoris, myocardial infarction, cerebral infarction, and revascularization) was recorded and compared between the two groups.

Statistical analysis

Statistical analysis was done using Statistical Packages for Social Sciences (SPSS Inc, Chicago, USA) for data processing while GraphPad Prism 7 (GraphPad Software, San Diego, CA, USA) for graphic presentations. Count data were presented as percentages (%), and analyzed using Chi-square test. Normally distributed continuous data were expressed as mean ± standard deviation (SD) and analyzed using independent samples t-test while paired t-test was used for intra-group comparisons. Multiple comparisons were done using ANOVA and tested using Post hoc Bonferroni test. Pearson test was conducted to analyze the relationship between CAS severity and bridge blood flow. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline patient data

There was no significant difference in age, body mass index, sex, course of disease, smoking history, hypertension, hyperlipidemia, diabetes mellitus, New York Heart Association (NYHA) classification, number of diseased coronary arteries and Gensini score between the two groups ($p > 0.05$) (Table 1).

Table 1: Baseline patient data

Parameter	Control group (n=47)	Study group (n=51)	χ^2/t	*P*-value
Age (years)	55.43±6.90	55.18±6.73	0.182	0.856
BMI (kg/m^2)	21.19±1.52	21.07±1.83	0.352	0.726
Sex			1.312	0.252
Male	30(63.83)	38(74.51)		
Female	17(36.17)	13(25.49)		
Course of disease (years)	2.70±0.91	2.47±0.78	1.346	0.181
Smoking history	26(55.32)	32(62.75)	0.558	0.455
Hypertension	36(76.60)	43(84.31)	0.932	0.334
Hyperlipemia	43(91.49)	48(94.12)	0.255	0.614
Diabetes mellitus	13(27.66)	11(21.57)	0.491	0.484
NYHA classification			0.772	0.856
Grade I	2(4.26)	1(1.96)		
Grade Ⅱ	27(57.45)	32(62.75)		
Grade III	15(31.91)	14(27.45)		
Grade IV	3(6.38)	4(7.84)		
No. of diseased coronary arteries			0.509	0.775
1-2	7(14.89)	8(15.69)		
2-3	24(51.06)	29(56.86)		
>3	16(34.04)	14(27.45)		
Gensini score	54.26±21.41	52.65±24.69	0.344	0.732

Note: BMI = body mass index), NYHA = New York Heart Association

Association between CAS severity and bridge vessel flow

A total of 37 patients were assessed to have severe stenosis (Gensini score ≥ 60 points), while the remaining 61 patients did not exhibit such stenosis (Gensini score < 60 points). Graft vessel flow rate was significantly higher in severe stenosis group compared to non-severe stenosis group ($p < 0.05$). The CAS severity and graft vessel flow rate demonstrated an inverse relationship ($r = -0.792$, $p < 0.001$) (Figure 1).

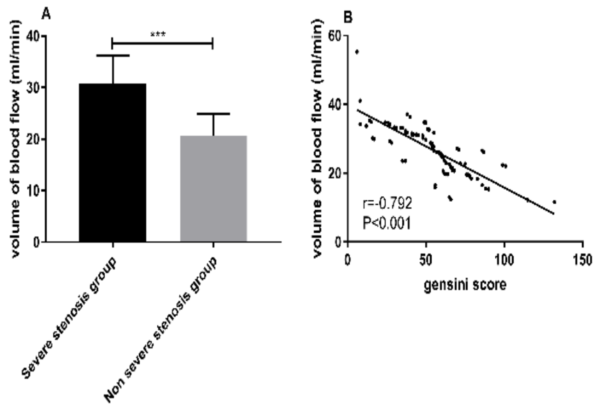

Figure 1: Association between different degrees of coronary artery stenosis and bridge vessel flow. ****P* < 0.05 vs. non-severe stenosis group

Changes in hemodynamics

At 12 h postoperative, HR, CVP, and MAP were significantly lower in study group compared to control group ($p < 0.05$). At 24 h postoperative, study group showed significantly lower CVP compared to control group ($p < 0.05$; Figure 2).

Total incidence of ACEs

There was no significant difference in overall incidence of ACEs 12 months after operation in both study and control groups ($p > 0.05$; Table 2).

1-year patency rate after operation

There was no significant difference in patency rate, mild stenosis rate, severe stenosis rate, complete occlusion rate and incidence of line-like sign in both study and control groups ($p > 0.05$; Table 3).

1-year patency rate

There was a significantly higher 1-year patency rate and lower incidence of line-like signs after operation in severe stenosis group compared to non-severe stenosis groups ($p < 0.05$; Table 4).

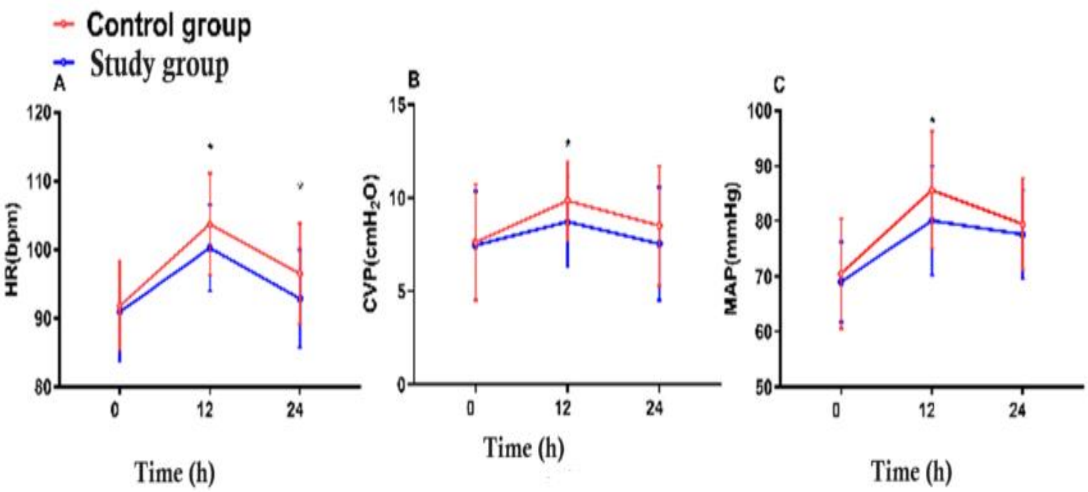

Figure 2: Changes in hemodynamic parameters, including heart rate (HR), central venous pressure (CVP), and mean arterial pressure (MAP) before and after surgery. **P* < 0.05 between study and control groups

Table 2: Overall incidence of adverse cardiovascular events

Parameter	Control group (n=47)	Study group (n=51)	χ^2	*P*-value
Revascularization	0(0.00)	1(1.96)		
Myocardial infarction	2(4.26)	1(1.96)		
Angina pectoris	3(6.38)	2(3.92)		
Cerebral infarction	2(4.26)	0(0.00)		
Total adverse cardiovascular events	7(14.89)	4(7.84)	1.145	0.285

Table 3: One-year patency rate after operation in the two groups

Parameter	Control group (n=47)	Study group (n=51)	χ^2	*P*-value
Patent	32(68.09)	41(80.39)	1.950	0.163
Mild stenosis	3(6.38)	1(1.96)	1.222	0.269
Severe stenosis	2(4.26)	2(3.92)	0.007	0.934
Complete occlusion	1(2.13)	1(1.96)	0.003	0.954
Line-like sign	9(19.15)	6(11.76)	1.029	0.310

Table 4: One-year patency rate after operation

Item	Severe stenosis group (n=37)	Non-severe stenosis group (n=61)	χ^2/t	*P*-value
Patent	32(94.56)	41(75.41)	4.502	0.034
Mild stenosis	1(2.70)	3(4.92)	0.289	0.591
Severe stenosis	1(2.70)	3(4.92)	0.289	0.591
Complete occlusion	1(2.70)	1(1.64)	0.130	0.718
Line-like sign	2(5.41)	13(21.31)	4.495	0.034

DISCUSSION

The main treatment methods for CHD include drug therapy, medical intervention and surgical treatment. Among these options, CABG has been found to have good long-term effects, high complete revascularization rate, low incidence of major cardio-cerebrovascular adverse effects and high survival rate [11]. As a result, a growing number of patients with CHD choose CABG for treatment. However, the patency of bridge vessels after CABG has always been a concern for clinicians. According to a previous study, when the internal mammary artery is anastomosed with the incompletely occluded coronary artery, the residual competitive flow within the coronary artery affects the patency of the bridge artery [12]. Additionally, the bridge artery is prone to contraction and spasm in the early stages after operation (often accompanied by competitive flow) and is visualized as a line-like sign under coronary angiography [13].

This study compared the graft bridge vessel flow in patients with varying degrees of CAS. The findings revealed significantly higher bridge vessel flow in the severe stenosis group compared to non-severe stenosis group. The inverse relationship between the severity of stenosis and graft vessel flow confirmed the presence of competitive flow. At 12 h postoperatively, study group exhibited significantly lower levels of HR, CVP, and MAP compared to control group. These reductions suggested a decrease in myocardial performance and oxygen consumption, indicating that diltiazem is beneficial for maintaining hemodynamics, reducing hemodynamic fluctuations, and decreasing cardiac preload and afterload in patients after CABG. Consequently, this drug may improve cardiac function. Toraman *et al* [14] compared the use of diltiazem, nitroglycerin and sodium nitroprusside in the treatment of CABG, and found that diltiazem provides better myocardial performance, stronger control of hypertension, and better hemodynamic stability. Moreover, no significant difference in the incidence of ACEs within one year after operation between the two groups, and overall incidence of ACEs was low in both groups.

Patency rate of graft vessels is a key indicator used to evaluate effectiveness of CABG [15]. This study revealed no significant difference between the two groups regarding graft patency rate, mild stenosis rate, severe stenosis rate, complete occlusion rate, and linear signs rate one year after operation. This is probably related to the stenosis at the proximal end of the target vessel. Multiple studies have indicated the degree of stenosis in the target vessel as one of the important factors influencing graft vessel patency [16]. When the bridging vessel is anastomosed with a target vessel that has a more severe stenosis, the patency rate tends to be higher. Conversely, when it is anastomosed with a target vessel with mild or moderate stenosis, patency rate decreases. This is because, the presence of a less stenosed target vessel increases competitive flow of blood to the bridge vessel, leading to a reduction in blood flow and diameter of the bridge vessel. This reduction is visualized as a line-like sign under coronary angiography. In this study, patency rate of bridge vessels within 1 year after operation was compared among patients with varying degrees of CAS, and the results revealed a significantly higher graft patency rate and lower incidence of linear signs in the severe stenosis group compared to non-severe stenosis group.

Hashimoto *et al* [17] suggested that a 60 % stenosis in the coronary artery may serve as a watershed for graft vessels, and competitive flow impact prognosis of graft vessels. These findings suggested that the severity of stenosis plays a role in determining graft patency rates after CABG.

Limitations of this study

This study has some limitations. Firstly, the limited number of cases collected in this retrospective study may compromise the generalizability of these results. Furthermore, specific outcome measures used in this study are limited, making it challenging to fully capture the results.

CONCLUSION

Postoperative administration of diltiazem in patients undergoing CABG significantly improves systemic circulation and hemodynamic parameters. However, competitive flow reduces the long-term patency rate of graft vessels in these patients.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Feng Cong and Xiangbin Meng conceived and designed the study, and drafted the manuscript. Feng Cong, Weidong Bing, Chengxin Liu, Xin Zhao and Yanwen Bi collected, analyzed and interpreted the experimental data. Xiangbin Meng and Yanwen Bi revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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