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Original Article

A correlation analysis of blood flow and CK-MB in coronary bypass grafting

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Abstract: In the clinical treatment of coronary heart disease, hemodynamic changes resulting from coronary artery blockage and the manipulation of vessels may lead to ischemia-reperfusion injuries on myocardial tissues. CK-MB is one creatine kinase that is often employed as a diagnostic marker of myocardial injury. However, the correlation between blood flow/pulsatile index during target vessel ligation is still unclear. The aim of this study was to investigate the relationship between blood flow/pulsatile index during target vessel ligation. The blood flow volume/waveform and the pulsatile index were measured using an instantaneous blood flow instrument. Chemiluminescence was used to determine the CK-MB levels in conjunction with a fully automatic immune analyzer. The correlation between blood flow volume or the pulsatile index of vessel ligation and CK-MB concentration 24 h after surgery was analyzed. There was a positive correlation between the CK-MB level and the blood flow volume/pulsatile index (correlation coefficient = 0.424 or 0.523) with a significant difference ($P<0.05$). The blood flow volume/pulsatile index is positively correlated with myocardial tissue injury. Therefore, the maintenance of circulation stability during surgery is of critical importance for alleviating myocardial injuries and improving cardiac function after surgery.

Keywords: Coronary artery bypass grafting, CK-MB, blood flow volume, pulsatile index

Introduction

With the transition of lifestyles and dietary habits, the age at which coronary heart disease (CHD) typically occurs is becoming younger in China. This trend is further aggravated by the aging of the whole population, which elevates the number of CHD patients in both the young and the aged [1]. Cardiac surgery has certain limitations, including general conditions and economic considerations. Therefore, the improvement of current treatment strategies can decrease healthcare costs for patients and for society as a whole, thus posing critical importance [2, 3].

Coronary artery bypass grafting is an effective method of treating CHD. Two major strategies are available, including the classical cardiopulmonary bypass-coronary artery bypass grafting and the newly developed off-pump coronary artery bypass grafting (OPCAB) [3]. The latter approach can protect cardiopulmonary function, decrease the probability of cardiac arrhythmia and in-surgery bleeding, and can lower the cost, making it a primary choice with increased safety [4]. A recent study showed that the maintenance of cardiac function and hemodynamic stability during coronary artery surgery can decrease the occurrence of complications, indicating an improved overall prognosis [5]. Therefore during OPCAB, the close monitoring of hemodynamics in the peri-operative period is of critical importance.

Creatine kinase (CK) is a critical enzyme in muscle energy metabolism. It can catalyze the phosphorylation reaction of creatine in a reversible process under physiological conditions [6]. CK has three isozymes, in which CK-MB is mainly located in the myocardial tissues, but with only trace amounts in the serum and other tissues. Therefore, CK-MB is frequently used as a diagnostic marker for cardiac injury [7]. Earlier studies suggested that the transient change of CK-MB is critical for acute cardiac infarction [8]. It has been reported that about 98% of all acute cardiac infarction patients have elevated serum

CK-MB levels. However, the correlation between CK-MB expression and the intra-operative hemodynamic pattern during OPCAB has not been described yet.

This study aimed to collect hemodynamic chart and serum CK-MB levels at 24 h after surgery from OPCAB patients in our hospital, and to analyze their correlations.

Materials and methods

Research objects

A total of 183 patients who received OPCAB surgery in Shandong Provincial Hospital Affiliated to Shandong University from November 2014 to December 2015 were recruited for this study. The inclusion criteria were determined based on the patient's medical history and a recent coronary artery angiogram. Those patients with a recent history of cardiac infarction, previous cardiac surgery, patients with pure left descending branch coronary artery disease, a valve malfunction, pulmonary artery disease, or other surgeries were excluded.

The study protocol was approved by the Research Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong University, and all the patients gave their informed consent before the study began.

Surgical plan

All included patients adopted their left internal mammary artery, radial artery, or great saphenous vein as the vascular bridge for RCA and LCX. During the surgery, LAD was firstly ligated, followed by the distal connection of RCA and LCX. The ligation between proximal RCA and LCX was performed at the end.

Hemodynamic monitor during surgery

During the surgery, a Medi-Stim Butterfly Flowmeter (Medstim, Oslo, Sweden) was used to record the hemodynamic pattern before and after LAD ligation, including blood flow volume, pulsatile index, blood flow waveform, heart rate, and ECG.

Serum CK-MB assay

Peripheral blood was collected from the patients and centrifuged to obtain the serum which was used to measure the CK-MB level using chemiluminescence, using a commercially available kit (Vitros, NJ, US) following the manual's instructions. 50 μl of diluted standard substance was added to each well to establish a standard curve. Next, 50 μl sample serum was added to the plate, which was washed five times, followed by measuring the OD value at 450 nm. The OD value of the standard substance was used to prepare a linear regression equation, which was adopted to calculate the samples' concentrations.

Statistical analysis

All data are presented as mean ± standard deviation (SD) and were processed using SPSS 19.0 software. The comparisons of the hemodynamic parameters at each step of the surgery were performed using a one-way analysis of variance (ANOVA). A paired *t*-test was used to compare the hemodynamic indexes before and after surgery. A Pearson analysis was adopted to check the correlation between CK-MB and the hemodynamic indexes. Statistical significance was defined when $P<0.05$.

Results

General condition of the patients

No deaths occurred among all the 185 patients. Three of them were diverted to cardio-pulmonary surgery due to the complexity of the anterior descending branch exposure and an unstable blood flow after the re-connection. Five cases had secondary open-chest surgeries due to bleeding. Two patients had re-bridging surgeries due to an unsatisfactory bridge flow rate. All patients were excluded from the observation group. The other patients had no complications during the surgery, nor did cardiac infarction during the peri-operative period nor did other severe complications occur. The patients had a relatively fast recovery and discharge.

Blood flow waveform and ECG during surgery

The Medi-Stim Butterfly Flowmeter instrument was used to measure the hemodynamic change of bridge vessels in real-time, including the basal levels before the induction of anesthesia, the levels during the distal connection of target vessels, and the proximal reconnection, and at the end of surgery. As shown in **Figure 1**, significant fluctuations were found at the time of the

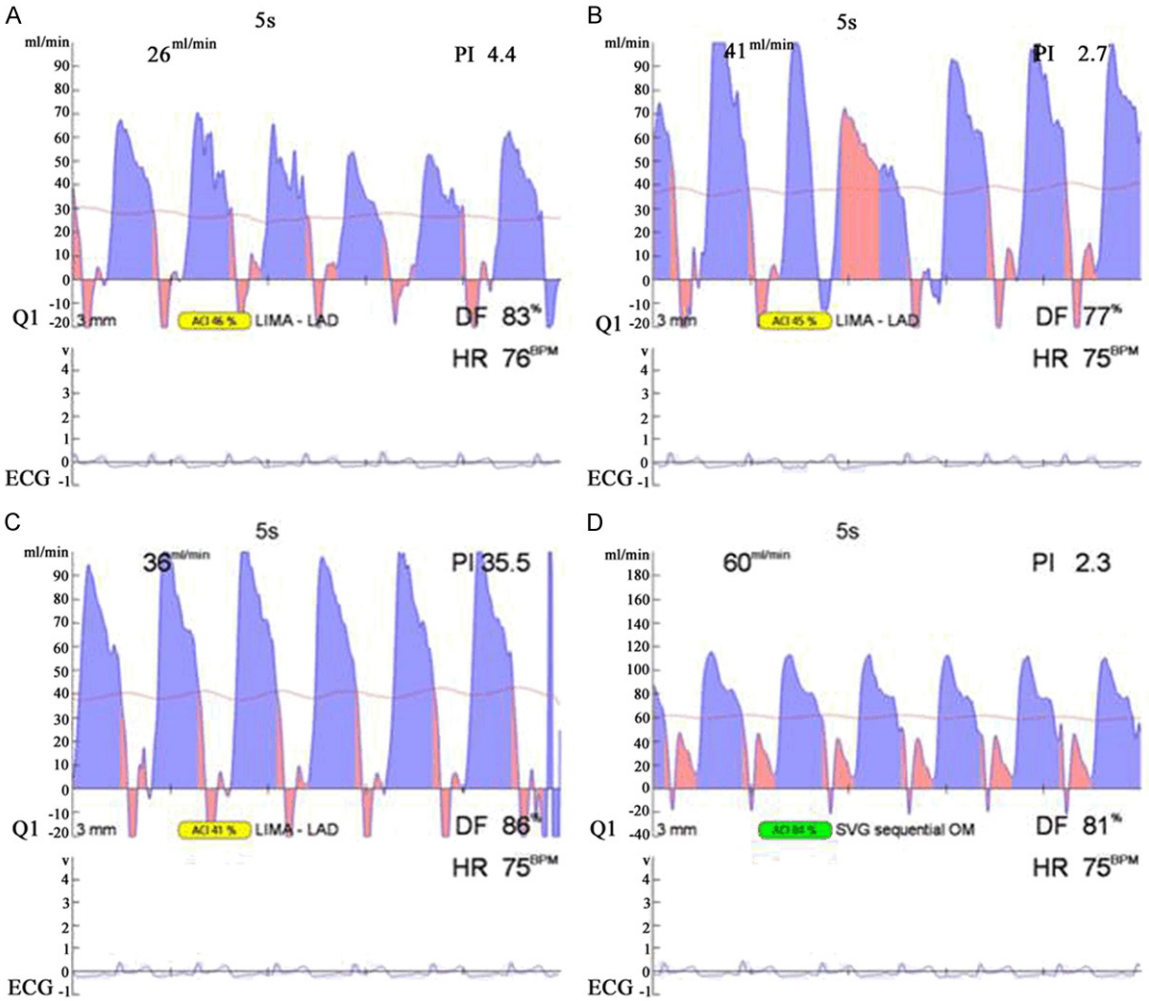

Figure 1. Representative images of patients' blood flow. A. After anesthesia induction; B. At the time of distal vessel reconnection; C. Completing distal connection; D. At the end of surgery.

Table 1. Hemodynamic index during surgery

	Anesthesia induction	Distal reconnection	Proximal reconnection	Surgery ending
Blood flow volume (mL/min)	26±6.28	41±9.21	36±9.89	60±14.55
Pulsatile index	4.4±2.14	2.7±2.29	35.5±6.45	4.2±4.11

target vessels' connections and distal connections, accompanied by a significantly increased pulsatile index. ECG, however, showed minor fluctuations with a smooth heart rate.

Hemodynamic indexes during surgery

The blood flow volume, pulsatile index, and blood flow wavelength were recorded in all 183 patients. Recorded during the four stages of monitoring, the blood flow volume and pulsatile index are shown in **Table 1**. During the targeted vessels distal connection process, there was a major fluctuation of blood flow volume. The pulsatile index, however, was relatively higher at the distal ligation of the targeted vessels.

CK-MB concentration at different time points

We employed a chemiluminescence approach combined with a Vitros 3,600 fully automatic immune analyzer to detect the serum CK-MB levels before, immediately after, 12 h, and 24 h after the surgery. As shown in **Table 2**, the post-

Table 2. CK-MB concentrations at different time points

Before surgery	Immediately after surgery	12 h after surgery	24 h after surgery	36 h after surgery	48 h after surgery
6.73±4.15	17.12±3.86*	18.87±2.47*	22.87±7.49*	19.65±12.13	14.92±12.87

All in μg/L, as the mean ± standard deviation; *, P<0.05.

Table 3. Correlation between blood flow volume/pulsatile index and CK-MB concentration

	Correlation coefficient	*P* value
Blood flow (mL/min)	R = 0.424	P<0.05
Pulsatile index	R = 0.523	P<0.05

operative CK-MB concentrations were significantly elevated after surgery and reached a peak level at 24 h (P<0.05).

Correlation between the hemodynamic index and CK-MB levels

From the CK-MB concentration and the hemodynamic changes at the different time points, it can be shown that the CK-MB level reached the peak 24 h after surgery. A correlation analysis showed a positive correlation of the CK-MB level at 24 h post-surgery with the blood flow volume or pulsatile index before/after the targeted vessel ligation (**Table 3**).

Discussion

OPCAB has several advantages over traditional cardiopulmonary bypass surgery, including no need to bypass circulation, no need to arrest the heart, both of which eliminate body injuries caused by non-physiological status such as low body temperature or non-pulsatile blood flow [9]. OPCAB surgery also has minimal invasiveness, thus decreasing cardiac trauma, as well as post-operative care, making it a popular choice currently [10].

The development of modern medical techniques has enabled us to monitor the fluctuations in blood flow during surgery in real-time. Recording the transient blood flow waveform can reflect the diastolic phase of the coronary artery, while the magnitude represents the perfusion of bridge vessels [11]. During OPCAB surgery, transient and significant hemodynamic changes occur due to the direct manipulation of the myocardial tissues [12, 13]. It is still unclear whether the maintenance of blood flow stability during surgery improves patient prognosis. This study utilized advanced equipment to record transient blood flow, including its volume, pulsatile index, and waveform. Blood flow volume can reflect the transient velocity of blood flow. The pulsatile index is a ratio calculated as the difference of blood flow between the systolic and diastolic phases divided by the average blood flow, and it is a reliable index for evaluating the quality of bridge vessels [13, 14]. A previous study showed that ischemia-reperfusion injury can lead to stress and apoptosis of the myocardial tissues [15], leading to myocardial injury. The change of blood flow and the pulsatile index may lead to ischemia-reperfusion such as injury to some extent [16]. Based on our surgical experiences, we hypothesized that the maintenance of blood flow stability could alleviate myocardial injury, although no study has mentioned this.

Previous studies showed a directly quantitative relationship between CK-MB levels and necrosis of the myocardial tissues [17-19]. This study thus selected CK-MB as the standard for evaluating myocardial injury, in order to study the correlation between the hemodynamic pattern and myocardial trauma during surgery. We recorded the hemodynamic indexes, mainly including the blood flow volume and the pulsatile index, and the CK-MB levels pre-/post-surgery were also quantified. We also measured the CK-MB concentrations before, immediately after, and at 6 h, 12 h, 24 h, and 48 h after each surgery. We found significantly elevated CK-MB levels immediately after surgery, and they reached a peak at 24 h. We thus selected the CK-MB value at 24 h for the correlation analysis, which revealed the relationship between the 24 h post-op CK-MB level with the blood flow volume/pulsatile index, with correlation coefficients at 0.424 or 0.523, respectively, with a significant difference. These results supported a strong correlation between the blood flow volume/pulsatile index and the 24 h post-op CK-MB level.

The blockage of coronary artery blood flow and circulation fluctuation as a result of blood vessel manipulation can cause ischemia-reperfusion injury [20], which can also cause myocardial injury, as shown by decreased left cardiac function after surgery [21]. Surgeons thus should have improved reconnection techniques to minimize the shape change of cardiac tissues due to force extension, to guarantee ligation suture, to minimize ligation time, and to reduce the sharp fluctuations in blood flow. The real-time monitoring of transient flow volume of bridge vessels can benefit the monitoring of surgical procedures, and can improve the quality of vessel ligation [22, 23].

Conclusion

Blood flow volume or the pulsatile index is correlated with the degree of myocardial injury, as shown by strong positive relationships. Therefore, transient blood flow monitoring and the maintenance of circulatory stability during surgery can help to reduce myocardial injury, improve post-operative heart function, and improve a patient's quality of life, and reduce medical costs. However, due to the limited number of patients enrolled in the present study, a large-cohort clinical study is needed to confirm the findings in the future.

Disclosure of conflict of interest

None.

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