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Effect of creatine kinase isoenzyme (CK-MB) on early prognosis after off-pump coronary artery bypass grafting.

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Keywords: coronary heart disease; beating coronary artery bypass grafting; myocardial enzymes; early prognosis.

Abstract. This study aimed to analyze the effect of elevated creatine kinase isozyme levels on early prognosis after off-pump coronary artery bypass (OPCAB) grafting. Based on the levels of creatine kinase isoenzyme (CK-MB), 116 patients were divided into two groups: one with a mild increase (n=85) and another group with a severe increase (n=31) in the enzyme. Clinical data, changes in CK-MB levels at 12, 24, and 48 hours after surgery, changes in left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVESD) before surgery, and seven days and three months after surgery were measured, and recorded. Also, the blood flow of the bridging vessel, vascular resistance, the diameter of the anterior descending branch, and the diameter of the distal target vessel were recorded during the operation (> 1.5 mm). A decrease in the level of LVEDD was recorded in both groups after the operation compared to the levels before. However, in the group with a mild increase in CK-MB, the LVEF after the operation increased compared to before the operation ($p<0.05$). The occurrence of angina pectoris 24 hours before surgery, high vascular resistance during surgery, and diameter of distal target vessel > 1.5 mm were related factors affecting the increase of CK-MB after surgery. The ratio of these factors was higher in the severe increase group than in the mild increase group ($p<0.05$). An increase in myocardial enzymes causes a slow recovery of myocardial function, so it can be used as a critical biological index to reflect the prognosis of patients.

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Efecto de la isoenzima de creatina quinasa (CK-MB) en el pronóstico temprano después de un injerto de revascularización coronaria sin circulación extracorpórea.

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Palabras clave: enfermedad cardiaca; injerto de revascularización coronaria con el corazón latiendo; creatine kinase isoenzyme (CK-MB); pronóstico temprano.

Resumen. Este estudio tuvo como objetivo analizar el efecto de los niveles elevados de la isoenzima de creatina quinasa (CK-MB) en el pronóstico temprano después de un injerto de revascularización coronaria sin circulación extracorpórea (OPCAB). Basados en el nivel de la isoenzima de creatina quinasa CK-MB, 116 pacientes fueron divididos en dos grupos: uno con un aumento leve de la enzima (n=85) y otro grupo con un aumento severo (n=31). Los datos clínicos, los cambios en los niveles de CK-MB a las 12, 24 y 48 horas posteriores a la cirugía, los cambios en la fracción de eyección del ventrículo izquierdo (LVEF) y el diámetro telediastólico del ventrículo izquierdo (LVESD) antes de la cirugía, 7 días y 3 meses después fueron medidos y registrados. Además, fueron registrados el flujo sanguíneo del puente venoso, la resistencia vascular, el diámetro de la rama descendente anterior y el diámetro del vaso diana distal durante la operación (> 1,5 mm). Se registró una disminución en el nivel de LVEDD en ambos grupos después de la operación en comparación con antes de la operación. Pero en el grupo con un ligero aumento, el nivel de LVEF después de la operación aumentó en comparación con el de antes (p<0,05). La aparición de angina de pecho 24 horas antes de la cirugía, la alta resistencia vascular durante la cirugía y el diámetro del vaso diana distal > 1,5 mm fueron los factores relacionados que afectaron al aumento de CK-MB después de la cirugía. La proporción de estos factores fue mayor en el grupo del aumento severo que en el grupo del aumento leve (p <0,05). Un incremento de las isoenzima de CK-MB provoca una recuperación lenta de la función miocárdica, por lo que puede utilizarse como un índice biológico crítico para reflejar el pronóstico de los pacientes.

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INTRODUCTION

Coronary heart disease is caused by blood flow obstruction caused by lumen stenosis based on coronary atherosclerosis, resulting in myocardial ischemia, hypoxia, or necrosis. Early, the patients have typical chest pain and dyspnea after fatigue or mood swings. If the obstruction cannot be relieved for too long, the patient may have cardiogenic shock at rest and even endanger the patient's life in severe cases [1,2]. In recent years, the incidence of coronary heart disease has increased and shows a younger patients' trend, and it has become a common disease seriously endangering people's health. Beating coronary artery bypass grafting is a frequent clinical cardiac surgery. It is of great value to improve the symptoms of myocardial ischemia, angina pectoris, and cardiac pumping function; nevertheless, it can cause mechanical damage to the heart during the operation. Postoperative complications such as arrhythmia and cardiac insufficiency often occur, so early detection of myocardium damage after surgery is critical for successful clinical treatment [3,4]. Creatine kinase isoenzyme (CK-MB) exists mainly in the myocardium but also in small amounts in normal blood and tissues outside the heart. When the myocardium is damaged, it can be released into the blood immediately and may be used in the clinic as a biomarker to reflect the degree of myocardial injury [5]a CK-MB standard is needed to eliminate between-method bias. Because the in vitro expression of human creatine kinase generates three isoenzymes, CK-MM, CK-MB, and CK-BB, it is important to establish an effective method to purify the isoform CK-MB from the mixture. In this study, we aimed at using tandem affinity purification (TAP. Related data show that early detection of myocardial CK-MB after surgery can significantly improve the occurrence of complications in patients, which has an essential role in the clinical treatment of coronary heart disease [6]. Therefore, by exploring the changes in postoperative CK-MB levels in patients with off-pump coronary artery bypass (OPCAB) grafting, this study aims to analyze the impact of elevated levels on early prognosis after this surgical procedure.

PATIENTS AND METHODS

General information

We selected 116 patients who underwent OPCAB grafting in our hospital from January 2018 to January 2019. The inclusion criteria were as follows: 1) the age was ≤ 90 years old; 2) all patients in whom the left internal mammary artery was used as the bridging vessel during the operation and bypass with the anterior descending branch; 3) ventricular ejection fractions > 50%; 4) patients and their families knew and signed a consent form. The hospital ethics committee approved this study. There were 86 males and 30 females aged 40 to 86 years (mean (63.58 ±7.69) years).

Operation method

The patient was in the supine position, and endotracheal intubation and ventilator-assisted ventilation were performed after general anesthesia. After entering the chest through the median sternal incision, the left internal mammary artery was removed with an intramammary retractor as a spare. The skin of the leg was cut open to expose the great saphenous vein from the 2cm above the medial malleolus. After pericardiotomy and suspension, the local myocardium to be anastomosed was fixed with Octopus cardiac fixator, the internal diameter of the anterior descending branch was measured and recorded, and the distal end of the great saphenous vein was anastomosed on the ascending aorta with suture. After each arterial bridge completed the kiss, the blood flow was measured and recorded by transient time flow. After the anastomosis of all bridges, the total time from the first to the last bridging vessels was recorded, and heparin was neutralized by protamine (1:1). The chest was closed layer by layer, and a drainage tube was placed in the pericardium and mediastinum.

After surgery, the patients entered the extracardiac intensive care unit and were continuously pumped with nitroglycerin for 24 hours. The changes in CK-MB levels were monitored at 12 h, 24 h, and 48 h after the operation. The patients whose highest value of CK-MB was ≤ 5.31ng/mL were included in the mild enzyme elevated group, and those with values > 5.31ng/mL were included in the severely elevated group. Patients were followed for seven days postoperatively.

Observation index

1) General data of all patients on admission were collected. These included age, sex, body mass index, hypertension, and diabetes history, previous myocardial infarction, 24-hour angina pectoris, and patients that had

undergone percutaneous coronary intervention (PCI). The blood flow of the bridge, vascular resistance, the diameter of the anterior descending branch, and the diameter of the distal target vessel were recorded during operation > 1.5mm.

2) Color Doppler echocardiography (PHILIPS SONOS5500) was used to detect the changes in the left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVESD) before the operation and seven days and three months after surgery.

Statistical method

Quantitative data of this study were expressed by ($\bar{x} \pm s$). The data of the mild and severe elevated groups were compared with the t-test. All the counting data were expressed by n (%). The χ^2 test tested the data comparison between the two groups, and the logistic regression analysis analyzed the related factors affecting the increase of postoperative CK-MB. $p<0.05$ was considered statistically significant. The IBM SPSS21.0 software package analyzed the data of this study.

RESULTS

Preoperative general data between the two groups

The incidence of angina pectoris 24 hours before operation in the severe elevation group was high (32.26%) when compared with that in the mild elevation group (9.41%), and the difference was statistically significant ($p<0.05$). The two groups had no significant difference in other data ($p>0.05$). See Table 1.

Comparison of CK-MB levels between the two groups during the perioperative period

The levels of CK-MB in the two groups were higher than that before the operation ($p<0.01$), and the peak of CK-MB appeared 12 hours after surgery- The level of CK-MB in the severe elevated group was higher than that in the mild elevated group at each time point after the operation ($p<0.05$). See Table 2.

Table 1

Comparison of preoperative isoenzyme values between the two groups.

General data	Mild elevation ≤ 5.31ng/mL (n=85)	Severe elevation > 5.31ng/mL (n=31)	t/χ^2	p
Age*	63.25±7.18	64.78±7.36	1.009	0.315
Gender (male/female)	63/22	23/8	0.001	0.993
BMI(kg/m²)*	23.67±3.12	24.55±3.29	1.325	0.188
Hypertension **	59(69.41)	20(64.52)	0.251	0.617
Diabetes **	35(41.76)	10(32.24)	0.761	0.383
Previous myocardial infarction **	30(35.29)	9(29.03)	0.399	0.528
Previous PCI **	7(8.24)	4(12.90)	0.576	0.448
Occurrence of angina pectoris 24 h before **operation	8(9.41)	10(32.26)	9.044	0.003
LVEDD (cm)*	5.67±0.37	5.58±0.59	0.978	0.330
LVEF (%)*	53.12±5.16	53.54±5.31	0.385	0.701

*($\bar{x} \pm s$), **[n (%)].

Table 2
Comparison of CK-MB levels between the two groups during the perioperative period.

Time	Mild elevation ≤ 5.31ng/mL (n=85)	Severe elevation > 5.31ng/mL (n=31)	*t*	*p*
Before operation (ng/mL)	0.93±0.54	0.90±0.53	0.266	0.791
12h after the operation (ng/mL)	2.26±0.85	10.77±12.77	6.153	<0.001
24h after the operation (ng/mL)	1.28±0.63	6.49±8.15	5.924	<0.001
48h after the operation (ng/mL)	0.86±0.49	2.57±1.52	9.199	<0.001

Values expressed as $\overline{x} \pm s$

Comparison of operation between the two groups

The proportion of patients whose diameter of the anterior descending artery ≤ 1.5mm and the diameter of the distal target vessel > 1.5mm in the severe elevated group were higher than those in the mild elevated group ($p<0.05$). The vascular resistance in the severe elevated group was significantly increased compared with that in the mild elevated group ($p<0.05$). See Table 3.

Logistic regression analysis of the related factors affecting the increase of postoperative CK-MB

Logistic regression analysis showed that the incidence of angina pectoris 24 hours before surgery, vascular resistance, and distal target vessel diameter > 1.5mm were related factors affecting the increase of postoperative CK-MB ($p<0.05$). See Table 4.

Comparison of cardiac function between the two groups before and after surgery

The level of LVEF three months after the operation in the mild elevated group was significantly higher than before surgery ($p<0.05$). In comparison, the level of LVEF at seven days and three months after operation in the severe elevated group was not significantly different from that before operation ($p>0.05$)- In contrast, the level of LVEDD seven days and three months after operation in the mild elevated group was significantly lower than that before operation ($p<0.05$). The level of LVEDD at three months after operation in the severely elevated group was decreased than before ($p<0.05$). See Table 5.

DISCUSSION

Currently, the clinical treatment of coronary heart disease is mainly by drug treatment, surgical treatment, and interventional stent treatment. Generally, different treatment schemes are chosen according to the severity of the patient's condition. Traditional coronary artery bypass grafting is performed under cardiopulmonary bypass, and the long-term typical rate of vascular anastomosis is high, as well as safety and effectiveness. However, cardiopulmonary bypass, cardiac arrest, and myocardial ischemia-reperfusion can cause systemic inflammatory reactions and multiple organ function damage, seriously endangering the life and health of patients [7]. In recent years, OPCAB surgery has entered a new period. During the operation, the anastomosis can be completed while maintaining the independent blood flow of the coronary artery and the beating heart, which reduces myocardial ischemia-reperfusion injury. Although the ascending aorta is not blocked during OPCAB grafting, the operation itself can cause myocardial ischemia-reperfusion injury during the anastomosis. Its effect on the prognosis of patients has become the focus of clinical schol-

Table 3
Comparison of surgery data between the two groups.

Operation condition		Mild elevation ≤ 5.31ng/mL (n=85)	Severe elevation > 5.31ng/mL (n=31)	t/χ^2	p
Internal mammary artery bridge flow (mL/min) *		30.12±13.58	29.58±17.11	0.135	0.788
Great saphenous vein bridge flow (mL/min) *		21.19±10.65	22.02±11.47	1.252	0.627
Vascular resistance (mmHg/mL/min) *		4.11±0.92	6.03±1.48	5.451	0.003
Diameter of the anterior descending branch	≤1.5mm **	6(7.06)	7(22.58)	5.500	0.019
	1.75~2.0 mm **	60(70.59)	18(58.06)	1.617	0.203
	≥2.25 mm **	19(22.35)	6(19.35)	0.121	0.728
Diameter of the distal target vessel	≤1.5mm**	65(76.47)	17(54.84)	5.130	0.024
	>1.5mm**	20(23.53)	14(45.16)	5.130	0.024

*($\bar{x} \pm s$), or **[n (%)].

Table 4
Logistic regression analysis of the related factors affecting the increase of postoperative CK-MB.

Variable	*B*	*SE*	*Wald* statistic quantity	*p*	*OR*	95%*CI*
Constant	-3.765	0.875	15.359	<0.001	0.022	
Vascular resistance	0.785	0.452	3.467	0.001	1.452	0.725~4.154
Occurrence of angina pectoris 24 hours before the operation	1.033	0.332	6.564	0.011	3.128	1.207~7.365
Diameter of the anterior descending branch≤1.5mm	0.688	0.428	2.211	0.127	2.113	0.663~6.280
Diameter of the distal target vessel >1.5mm	0.402	0.153	5.610	0.015	1.461	1.063~2.142

Table 5
Comparison of cardiac function between the two groups before and after surgery.

Cardiac function	Group	Before the operation	Seven days after the operation	Three months after the operation
LVEF (%)	Mild elevation	53.12±5.16	53.84±5.13	57.48±5.01*
	Severe elevation	53.54±5.31	54.63±5.22	54.32±6.15
LVEDD (cm)	Mild elevation	5.67±0.37	4.73±0.35*	4.74±0.39*
	Severe elevation	5.58±0.59	5.02±0.36	4.78±0.49*

Note: compared with pre-operation * $p < 0.05$

Values expressed as $\bar{x} \pm s$

LVEF left ventricular ejection fraction; LVEDD left ventricular end-diastolic diameter.

ars [8,9] we revised 400 patients; 200 received on-pump CABG and 200 off-pump OPCAB (OPCAB. OPCAB grafting consists of revascularization of bridging blood vessels, which can be improved by distal coronary artery obstruction and stenosis, so myocardial ischemia-reperfusion injury will inevitably occur after the operation [10]. Keeping a clear field of vision for the operation during vascular anastomosis will temporarily block the proximal vessels, resulting in temporary ischemia of the muscles dominated by the distal end of the artery. A significant decrease in blood pressure during the operation can cause arterial vasospasm and then cause myocardial ischemic injury. If the patients do not move in time after sorgery, it is easy to form coronary or bridging vascular thrombosis, resulting in myocardial ischemic injury and a significant increase of myocardial enzymes [11].

CK-MB is a kind of myocardial enzyme mainly present in cardiomyocytes' cytoplasm. As an essential enzyme detection index of myocardial injury, it has been paid more and more attention in clinical practice [12]. The content of CK-MB in serum is minimal. Generally, the cell membrane permeability increases after myocardial injury, and its level in the blood peaks after nine to 30 hours. Therefore, CK-MB detection is often combined with clinical symptoms and cardiac echocardiography to evaluate the severity of myocardial injury [13]the rats received ISO subcutaneously at a dose of 100 mg/kg for three days. In group III, rats received ISO as group II and then GNPs (400 μg/kg/day). In this study, by examining the postoperative CK-MB level, the patients with the highest value ≤ 5.31ng/mL were included in the slightly elevated group (mild elevated group) and those with levels > 5.31ng/mL were classified as the significantly elevated (severe elevated group). Based on the analysis of the data of the two groups, it was found that the peak level of CK-MB appeared 12 hours after the operation, and the level of CK-MB in the severe elevated group was significantly higher than in the mild elevated group at each time point after surgery ($p<0.05$). In addition, the Logistic regression analysis results showed that the occurrence of angina pectoris 24 hours before operation, high vascular resistance, and distal target vessel diameter > 1.5mm were related factors affecting the increase of postoperative CK-MB ($p<0.05$). The related data show that the blood flow of the bridge is positively correlated with the diameter of the distal coronary artery. When there is stenosis or obstruction of the distal vessel, the anastomotic site is not unobstructed and the blood flow is small [14]. The positive correlation between the diameter of the distal target vessel > 1.5mm and the increase of CK-MB may be due to the decrease of blood flow caused by a large vascular plaque load, which in turn affects the increase of CK-MB level [15]each of whom presented with a normal ECG and was subjected to emergency coronary angiography (CAG).

This study showed that the improvement degree and speed of LVEF and LVEDD were different in patients with different levels of CK-MB after OPCAB grafting. The level of LVEF in patients with mild elevation was significantly higher than that before the operation and three months after the operation ($p<0.05$); the level of LVEDD in the mild elevated group was significantly lower than that before the operation at seven days and three months after operation ($p<0.05$); the level of LVEDD in severe elevated group was significantly lower than that before operation and three months after operation ($p<0.05$). This finding suggests that the higher the level of CK-MB after surgery, the longer the duration, the more serious the myocardial injury of patients, and the worse the prognosis.

To sum up, angina pectoris attack, distal target vessel diameter > 1.5mm, and elevated vascular resistance before beating coronary artery bypass grafting can affect the elevation of myocardial enzymes after the operation, and the recovery of myocardial function is slow in patients with significantly increased myocardial enzymes, which can be used as an essential biological index to reflect the prognosis of patients.

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Competing Interests

The authors declared that they have no competing interests.

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Authors' Contribution

Conception and design: Z Z: Administrative support; LW: Provision of study materials or patients; ZZ, JW: Collection and assembly of data; NL, YL: Data analysis and interpretation; LS: Manuscript writing; All authors: Final approval of manuscript.

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