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·论著·

心脏移植患者围手术期心肌肌钙蛋白Ⅰ的动态变化

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摘要：目的 观察心脏移植患者围手术期心肌肌钙蛋白Ⅰ(CTnⅠ)的动态变化,了解心脏移植中心肌保护的效果及术后心脏损伤恢复的情况。方法 测定 5 例心脏移植患者术前、手术当日及术后(1~17)天心肌肌钙蛋白Ⅰ的变化。供心植入前采用 StThomas液保护, 植入中用冷血保护。结果 心脏移植患者与供者术前 CTnⅠ基本在正常范围,手术当日及术后 CTnⅠ较术前升高,然后逐渐下降,于第 12 天恢复在正常值范围内。第 2 例患者停机后对鱼精蛋白过敏又二次转流,术后 CTnⅠ较其他 4 例患者峰值高且下降速度慢,于术后第 21 天死于脏器衰竭,另 4 例患痊愈出院。结论 心肌肌钙蛋白Ⅰ在心脏移植当日及术后明显高正常值,术后第 12 天基本正常水平。心肌肌钙蛋白Ⅰ明显升高也表明供心的心肌保护仍存在着缺陷。

关键词： 心脏移植;心肌肌钙蛋白Ⅰ;供心保护;体外循环
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Dynamic change of cardiac troponin Ⅰ for heart transplantation in perioperative period

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Abstract: Objective: To observe the dynamic change of cardiac troponin Ⅰ (CTnⅠ) of heart transplantation patients in perioperative period, and to understand the effect of myocardial preservation for heart transplantation and the recovery of the heart being operated on. **Methods:** The cardiac troponin Ⅰ of five patients with heart transplantation was measured the day before operation, on the operating day and from the first day to the 17th day after operation. The donor heart was preserved in St.Thomas before transplantation and in cold blood whiling transplanting. **Results:** The CTnⅠ was basically in normal scope before operation. On the transplanting day and after the transplantation, the CTnⅠ increased and then gradually decreased and it turned to normal on the 12th day after the transplantation. The second patient had allergy reflect and took second perfusion after the machine was stopped, after operation the CTnⅠ peak value was higher than the other four patients and the CTnⅠ deceased slowly and died of multi-organ failure 21 days after transplantation and other 4 patients left hospital after recovery. **Conclusions:** The CTnⅠ value was obviously higher on the transplanting day and after the day than the day before operation and it turned to normal on the 12th day after transplantation. This shows that the preservation of the donor heart has some defects.

Key words: heart transplantation; myocardial troponinⅠ; donor heart myocardial preservation; cardiopul-

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The preservation effect of donor heart determines the success of transplantation and long-time quality of life. Our department had practiced heart transplantation for five patients from Jan. 2001 to May 2001. Among them, one patient died of multi-organ failure in twenty days after operation, other patients have stock up to now, the cardiac troponin I values of the five patients in perioperative period were reported as follow.

1 Objects and methods

1.1 Objects

For five cardiac disease patients, four male patients were dilataltion cardiomyopathy, one female patient was endemic cardiomyopathy. Their ages were 27, 18, 41 and 53 years; their body weights were 71, 49, 64, 60 and 65 kg. The donators' age corresponding the patients age were 27, 24, 21, 25, 23 and their body weights corresponding the patients' body weights were 72, 65, 76, 55 and 75 kg. All the five donators were train death. Each donator's blood type matches with that of the patient. Their Giant Cell viruses, FB virus, hepatitis virus were all negative. The body weight ratio of donors to receptors were 72/70, 65/49, 76/64, 55/60 and 75/65; the age ratio of donors to receptors were 27/29, 24/18, 21/41, 25/21 and 23/53.

1.2 Method of myocardial preservation for donor hearts

For the five donors´ bodies, 2.5 mg/kg heparin was given to each of them for the purpose of anti-blood coagulation, and 500 mg of methylprednisolone were injected to each of them through vein. After splitting breastbone, we opened pericardium by down "T" form, separated superior vena cava and inferior vena cava and put interruption tape under aorta root, and then inserted cold perfusion cube through aorta. After blocked aorta, (1200~1500) mL of 4℃ crystal cardioplegia (contain K^+ 28 mmol/L, neoton 2.5 g/L) were perfused through aorta root. We took out donor's heart, coated it with carbasus and put it into container with sterile water to transport. During transport period, 500 ml cold cardioplegia was perfused by aorta toot every 15 minutes. In the period of clipping donor hearts, they were also put into the cold water. During the process of transplanting, the donor hearts were protected by the cold blood cardioplegia that was made by mixing the cold crystal cardioplegia to the patients' own blood by the ratio of 1:4. Meanwhile, 2.5 g/L of neoton was added in cold blood cardioplegia. The cold blood cardiopegia was pulled on the donor hearts every twenty minutes.

1.3 Methods of prime and perfusion of extracorporeal circulation

Jostar membrane oxygenato was used for all patients to conduct the extracorporeal circulation. The priming fluid included: acetic acid sodium equilibrium liquid, man-made plasm or human plasm, human serum albumin, 4% $NaHCO_3$, 20% mannite and methylprednisolone. The ultrafiltration assembly has been used for all the five patients in extracorporeal circulation. The second patient's blood pressure decreased suddenly and his heart inflated after stopping extracorporeal circulation and then using protamine and heparin, which were assisted to circulation by using extracorporeal circulation again for nineteen minutes. When the blood pressure and cardiac rhythm came to normal, the extracorporeal circulation was stopped. The related markers of extracorporeal circulation for five patients are shown in Table 1.

1.4 Method of immunosuppressive therapy

The FK-506, mycopenolate mofetil and methylprednisolone were used for five patients in immunosuppressive therapy. The dose of FK-506 was (0.11~0.3) mg/kg every day. The dose was adjusted according to the ravine worth of drug concentration in blood (the standard is 15~20 μg/L). The mycophenolate mofetil dose was 1 g twice a day. The methylprednisolone dose was 150 mg per

Table 1 Markers of extracorporeal circulation for five patients

Markers of CPB	1st case	2nd case	3rd case	4th case	5th case
Perfusion flow (L/m²/min)	1.9~2.1	1.8~2.1	3.2~3.4	2.3~2.5	2.1~2.3
Perfusion pressure (mmHg)	58~78	48~80	46~78	48~88	45~84
Lowest nose T (℃)	27	27.1	24.4	29	28.8
Perfusion time (min)	210	137	103	138	190
Aorta block time (min)	78	87	103	68	112
Open aorta nose T (℃)	31	30	31.6	31	33
Stat of heart re-beating	auto	auto	auto	auto	auto
Stop CPB nose T (℃)	37.0	37.0	37.0	37	36.7
Urine volume in CPB (mL)	900	1000	100	0	600
Ultrafiltrate volume (ml)	500	2000	2500	3000	3000

day for ten days, then meticorten 1 mg/kg was used per day to replace the methlprednisolone. The total dosage of meticorten was reduced progressively by 5 mg a day. Immunological rejection didn't appear in five patients, and those drugs had no side effects. The effect of immunosuppression was precise and stable.

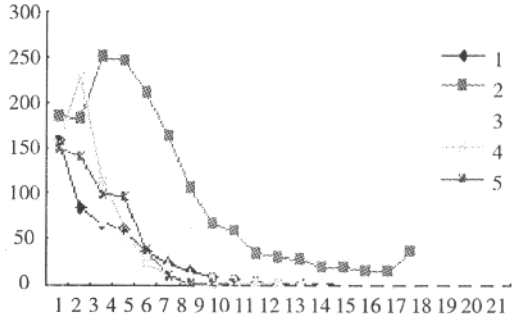
1.5 Methods of sample collecting and measuring

The blood was collected for examination everyday before transplantation, on the day of transplanting and after transplantation. CTn Ⅰ was measured by access. The normal CTn Ⅰ value in blood serum was based on the standard[1] CTn Ⅰ ≤3.1 μg/L.

2 Results

The extracorporeal circulation perfusion time for five patients was respectively 210, 183, 137, 138 and 190 min; aorta block time was respectively 78, 103, 87, 68 and 112 min. After the aorta block clip was opened, five donors' hearts all re-beating by themselves, and their rhythm showed sinus rhythm. During the extracorporeal circulation, their perfusion pressure was kept at (68~88) mmHg, and their urine volume range was (0~1 000) ml. All patients used ultrafiltration device to filter out the supernumerary liquid in patients' body, the ultrafiltrate volume range was (500~3 000) ml. From the second day after transplantation, the second patient had oliguria and anuresis. The continuous renal replacement therapy (CRRT) was used for seventeen days, but the patient died of multiple organ failure. Only one patient didn't have his CTn Ⅰ measured, the other four patients' CTn Ⅰ range before transplantation was (0~2.6) μg/L. The respective changes of the five patients' CTn Ⅰ after transplantation are shown in diagram Ⅰ.

Diagram: Changes of CTn Ⅰ for five heart trans plantation patients



3 Discussion

Cardiac Troponin is made up of cardiac Troponin T, Cardiac Troponin Ⅰ and Cardiac Troponin C, which adjusts myocardium contraction. CTn Ⅰ is one part of Troponin Complex. It is a kind of uni-chain polypeptide. Its antigenictity is obviously different from that of skeletal muscles, and its polyclonal antibody in blood serum could get rid of crossing response with skeletal muscles after going through immunoabsorption. Its peculiarity could be 100%. During myocardial necrosis, CTn Ⅰ could be released to blood through cell membrane. CTn Ⅰ has three different kinds of form, which respectively fix in skeletal muscles swift-muscle, sketetal muscle slow-muscle and myocardium. Among them,

the CTn Ⅰ weight, amino acid conformation and immunology specificity in myocardium molecule are all different from those of the two forms of CTn Ⅰ in skeletal muscles. When skeletal muscles are injured, the CTn Ⅰ does not show. It only rises when myocardium is injured. For heart, CTn Ⅰ is more specific than CTn T, it is specifically sensitive marker for myocardium injury. After acute myocardial infarction, the time when CTn Ⅰ appeared was similar to that of CK-MB. Their average time was 6.8 h, and CTn Ⅰ reached its peak at 11.2 h, but lasted for quite a long period of time, about 99 h. After acute myocardial infarction, its concentration in plasm could last for five to seven days, so it is not easy to make mistakes in measurement. The specificity of CTn Ⅰ was 100% in measuring cardiac muscle cell necrosis. Compared with myocardium enzyme in blood serum, CTn Ⅰ is a more peculiar, more sensitive marker for myocardium injury. It can be used to examine the minor myocardial damage in heart during operation. Moreover, it can be used as an earlier marker that can make up for each other's disadvantages by using their own advantage to evaluated left ventricle function and coronary artery recanalization. The specificity of CTn Ⅰ can be checked out as a marker to show the ischemic myocardium injury by immunology method.

In recently years, many scholars abroad [2~4] have already regarded cardiac troponin as an evaluation standard of the myocardial preservation during operation on heart. For the five patients in this group, only one patient's CTn Ⅰ was not be measured before operation, the other four patients' CTn Ⅰ was in normal value before operation. During the process of donor heart transplantation, the donor hearts' CTn Ⅰ concentrations were increased in receptor blood serum due to the donor heart's injure for the lack of blood; thus the CTn Ⅰ raised obviously during that day of operation and after operation. It is reported[5] that the increase and decrease of the cardiac troponin T value had obviously positive correlation with aorta blockage time. Jiang JP[6] reported that the CTn Ⅰ before operation increased by 5.8~15 times than CTn Ⅰ after operation for operation on heart's patients with extracorporeal circulation, but he thought that the discrepancy of CTn Ⅰ after operation had nothing to do with operation time and aorta blockage time. Judging from the aorta blockage time and the changes of CTn Ⅰ in our five patients, the fifth patient's aorta blockage time was the longest, after operation the highest peak of his CTn Ⅰ was 226.7 μg/L, and the CTn Ⅰ of the second patient increased obviously on the third day after operation and decreased from the fourth day. The increase of the CTn Ⅰ peak and its slowly decrease may be related to protamine hypersensitivity and myocardium injury resulted from the second time extracorporeal circulation. After operation the other three patients' cold ischemia time was less than the fifth patient's, and their CTn Ⅰ peaks were lower than the fifth patient's too. Antman EM[7], while comparing the relationship between the CTn Ⅰ of instable cardiac angina and myocardial infarction and death rate, he thought that the death rate of the patient whose CTn Ⅰ ≥0.4 ng/ml was significantly higher than that of those whose CTn Ⅰ ≤0.4 ng/ml. Furthermore, the death rate would greatly increase once CTn Ⅰ increased by 1 ng/ml.

In China, different methods of myocardial preservation for heart transplantation had been applied and their results were also different[8~10]. The donor hearts were preserved using St. Thoms Ⅱ with neoton 5 g/L (K^+ concentration was 28 mmol/L) about 4~6℃ for this group of patients, and the cardioplegia was perfused in aorta root. During this period, the cardioplegia didn't concern with the extracorporeal circulation priming fluid volume, so ultra-dosage cardioplegia could be used for the donor heart to guarantee its low temperature and cardioplegia sufficient perfusion. During the process of transplanting, the donor hearts were protected by the cold blood cardioplegia that was made by mixing the cold crystal cardioplegia to the patient's own blood by the ratio of 1:4. the K^+ concentration

was 20 mmol/L; cardioplegia volume was 500 ml per time and the time between two perfused cardioplegia was 20 minutes. All the five donor hearts were re-beating by themselves after 96 to 122 minutes' of blood shortage, and their cardiac function and circulatory system were in relatively stable condition after operation. These show that myocardial preservation is effective. However, some defects could be found in myocardial preservation in this method the measured result of CTn Ⅰ, that is CTn Ⅰ after operation was higher.

CTn Ⅰ is regarded as a judging standard for irreversible myocardium injury. By analyzing the detected result of the five patients, we thought that the myocardial preservation was well done when CTn Ⅰ was less than 170 μg/L. for the four surviving patients, the CTn Ⅰ of the first patient reached 266 μg/ml on the third day after transplantation, and on the fourth day his CTn Ⅰ decreased to 114.1 μg/L. We thought that the detection result might have some errors. The CTn Ⅰ range of the second patient in the first six days after transplantation was (249.6~160.0) μg/L, and it lasted for quite a long time. We thought there might be two reasons: one was that, for this patient, after stopping exreacorporeal circulation, the use of protamine and heparin resulted in cardiac rhythm disorder and blood pressure decrease, thus led to myocardium injury; the other reason was the patient's unobvious rejective reaction after operation. As for the question that how much CTn Ⅰ could be regarded as a standard for judging that the myocardium has been severely injured which thus affects the patient's survival after operation, it still needs further research.

References:

[1] WANG SW, QIAN FY. Chief editor. Old-Age cardiology[M]. BeiJing: The People Public Health Publishing Company, 1998: 388-389.

[2] Uchino T, William-Olsson G, Ishimaru S, et al. Estimation of Myoacrial Damage After Cardiac Surgery by Myosin Light Chain I and Troponin T[J]. Kyobu-Geka, 1994, 47 (12): 965.

[3] Knoth C, Boldt J, Dehne M, et al. Comparison of different prophylactic myocardium saving measures during heart surgery. Effects on preoperative Troponin T levels [J]. J Cardiovasc Surg, 1996, 37 (4): 367.

[4] Vecchia LL, Mezzena G, Ometto R, et al. Detectable serum troponin Ⅰ in patients whith heart failure of non myocardial ischemic origin[J]. Am J Cardial, 1997, 88(1):88-90.

[5] Wang YJ, Cai HW, Chen JH, et al. Changes of serum cardiac troponin T in patients undergoing cardiol surgery[J]. Hunan Yike Daxue Xuebao, 1999, 24 (1): 41-43. Chinese

[6] JIANG JP, WANG ZY, TAN BZ, et al. Dynamic observation of serum CTn Ⅰ in extracorporal circulation [J]. Jiangxi Yixue Jianyan, 1998, 11 (2): 70-73.

[7] Antman EM, Grudzien C. Evaluation of rapid bedside assay for detection of serum cardiac troponin Ⅰ [J]. JAMA, 1995, 273: 1279.

[8] ZANG WF, XIA QM, CHEN ZD, et al. Analysis on the therapeutic effects of orthotopic heart transplantation in 3 cases [J]. Zhonghua Qiguan Yizhi Zazhi, 1997, 18 (2): 66-68. Chinese

[9] WANG CS, HONG T, ZHAO Q, et al. Preliminary experience of Ⅱ successful orthotopic heart transplantations [J]. Zhohnghua Xinxueguan Bing Zazhi, 2002, 30 (1): 43-45. Chinese

[10] Li LS, Cai ZJ, Wang XW, et al. Supervision and management of perioperative changes in cardiovascular function in heart allotransplantation[J]. Disi Junyi Daxue Xuebao, 2002, 23 (20): 1892-1895. Chinses

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relationship to the tissue inhibitors of metalloproteinases and membrane type- 1-matrix metalloproteinase [J]. Br J Cancer, 2001, 84:1664-1670.

[14] Reid HM, McElligott AM, McGlynn H. Phertotypic alterations in Caki-1 Cells as a consequence of TIMP-1 overexpression [J]. C.Ancer Lett, 2001, 169: 189-198.

[15] Strongin AY, Collier I, Bannikov G, et al. Mechanism of cell surface activation membrane metalloproteinases[J]. J Biol Chore 1995, 270: 5331-5338.

[16] Zucker S, Hymowitz M, Conner C, et al. Measurement of matrix metalloproteinases and tissue inhibitors of metalloproteinases in blood tissues[J]. Ann N Y Acad Sci, 1999, 878: 212-227.

[17] Matsuyama Y; Takao S, Ailou T. Comparison of matrix metalloproteinases expression between primary tumors with or without liver metastasis in pancreatic and colorectal carcinomas [J]. J Surg Oncol, 2002, 80: 105-110.

[18] Garbett EA, Reed MW., Brown NJ, et al. Proteolysis in human breast and colorectal cancer[J]. Br J Cancer, 1999, 8: 287-293.

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