

Clinical Study of Myocardial Protection During Open Heart Surgery

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Introduction

It is generally agreed that the best method of myocardial protection is to keep natural perfusion of the myocardium throughout the operation. However, cardiac surgery frequently requires the interruption of the coronary circulation to allow the surgeon to operate upon a quiet and bloodless heart for precise repair of cardiac defects. In an effort to reduce ischemic damage to the myocardium during surgery, various methods have been employed as compatible with technical advantages in a variety of cardiac surgical procedures.

It is of great importance to compare the effect of current techniques for myocardial protection, because myocardial damage is the most frequent cause of death after surgery. Since there is no single ideal method for assessing the effect of myocardial protection in a variety of conditions in each case, it is difficult to determine the advantages of one method

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over another on a clinical basis. This might be possible only by analyzing a large series of the patients.

In this report, open heart operations performed during the past 12 years are evaluated retrospectively from the standpoint of myocardial protection.

Material and Method

Data were obtained retrospectively from the operative records of 3568 patients treated by cardiac surgery during cardiopulmonary bypass at Kyoto University Hospital and affiliated hospitals (Tenri Hospital, Hyogo Kenritsu Amagasaki Hospital, Himeji National Hospital and Kokura Memorial Hospital) from January, 1965, through September, 1977 (Table 1).

Table 1 Mortality related to the type of heart disease. "Other" indicates a combination of more than one defects.

Type of Heart Disease	Case	Early Death	Mortality (%)
ASD	700	21	3.0
VSD	1150	61	5.3
TOF	476	81	17.0
TGA	46	24	52.2
AVD	128	26	20.3
MVD	313	37	11.8
CAD	46	2	4.3
Other	707	83	11.7
Total	3568	335	9.4

ASD : Atrial Septal Defect
VSD : Ventricular Septal Defect
TOF : Tetralogy of Fallot
TGA : Transposition of Great Arteries

AVD : Aortic Valve Disease
MVD : Mitral Valve Disease
CAD : Coronary Artery Disease

On the basis of the method of myocardial protection, surgical techniques were divided into three groups : the aorta was not clamped (Group 1), the aorta was clamped (Group 2) and the coronary arteries were selectively perfused (Group 3). Each group included a variety of diseases. Some were single defects, others were combined diseases categorized as "other" (Fig. 1). Artificial ventricular fibrillation and local (by cold saline or ice slush) or systemic (by cardiopulmonary bypass) hypothermia were utilized in conjunction with the above techniques. Deep hypothermia with limited cardiopulmonary bypass (Kyoto technique) was not included in this study because this method is indicated only in small infants.

The effects of hemodilution and steroid therapy during cardiopulmonary bypass were also examined.

These techniques were assessed on the basis of 1) restoration of rhythmic contraction following anoxic arrest (spontaneous defibrillation), 2) inotropic support during and after

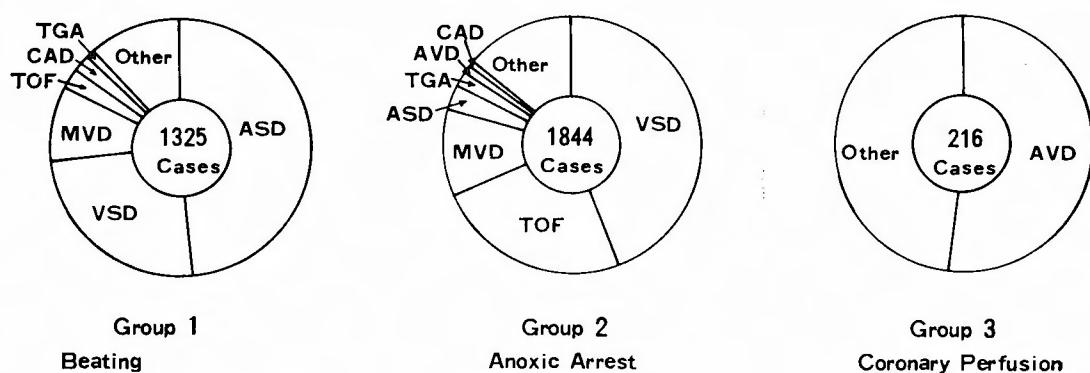


Fig. 1 Composition of the Groups. "Other" means a combination of more than one defect.

bypass, 3) prolonged assisted circulation (longer than 60 minutes) before weaning off bypass and 4) early death.

Result

The result are summarized in Tables 1, 2 and 3, and Figures 1 through 7 (The number of cases is different in each table because of incomplete recording of some of the parameters). In most instances, the surgical technique was chosen according to the type of disease, but in some two different methods were used (Table 2). There were no significant differences in early mortality between the two methods. The overall results of these techniques are shown in Table 3. The mortality rate was lowest in Group 1 and highest in Group 3. No significant effect of artificial ventricular fibrillation or local cardiac cooling was noted in any of the groups.

The elective period of simple anoxic arrest was assessed on the basis of spontaneous restoration of rhythm after coronary reperfusion, use of inotropic drugs and early death

Table 2 Mortality related to surgical procedure.

Heart Disease Procedure	ASD	VSD	TOF	TGA	AVD	MVD	CAD
Group 1	$\frac{14}{544}$ (2.6%)	$\frac{12}{284}$ (4.2%)	$\frac{6}{19}$ (31.6%)	$\frac{4}{6}$ (66.7%)		$\frac{12}{84}$ (14.2%)	$\frac{2}{32}$ (6.3%)
Group 2	$\frac{5}{49}$ (10.2%)	$\frac{39}{715}$ (5.5%)	$\frac{66}{388}$ (17.0%)	$\frac{19}{31}$ (61.3%)	$\frac{2}{9}$ (22.2%)	$\frac{20}{160}$ (12.5%)	$\frac{0}{9}$ (0%)
Group 3					$\frac{23}{91}$ (25.3%)		

Early Death/Number of Case (Mortality)

Table 3 Overall result related to surgical procedure.

		Case	Inotropic Support (%)	Long Assisted Bypass (%)	Inability to Wean off Bypass (%)	Early Death (%)
Group 1	Beating	876	22.2	1.1	0.5	5.0
	VF	277	(21.5) 19.3	(1.0) 0.9	(0.5) 0.4	(5.5) 7.5
Group 2	AC	1415	31.7	4.9	2.5	11.6
	AC+TC AC+VF	37 157	30.0 (32.3) 38.6	8.1 (5.3) 7.6	0 (2.3) 1.3	13.9 (120) 15.5
Group 3	CP	137	33.1	10.4	6.3	24.0
	CP+TC	28	25.0 (31.4)	3.6 (9.7)	3.6 (6.5)	32.1 (25.7)
	CP+VF	14	28.6	14.3	14.3	28.6
Total		2938	27.8	3.9	1.9	10.3

VF Electrical Ventricular Fibrillation, AC Simple Aortic Clamp, TC : Topical Cooling
CP : Coronary Perfusion, () : Group Average

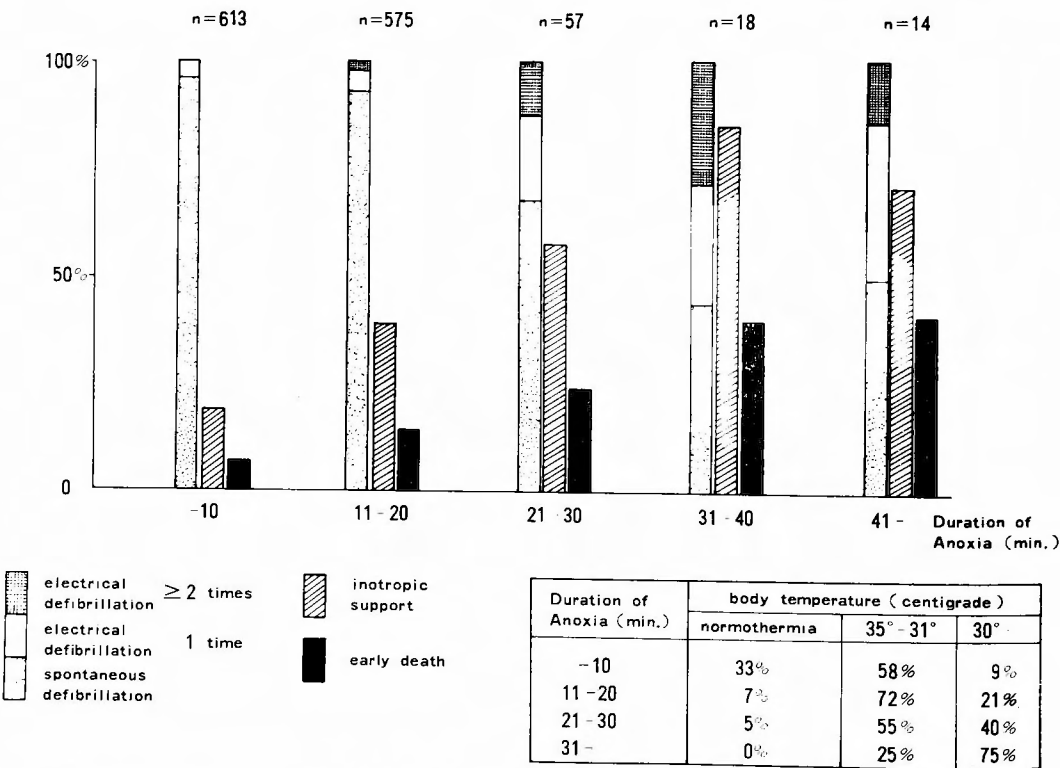


Fig. 2 Simple anoxic arrest and duration of anoxia. The table (below) shows the distribution of body temperatures in each period of anoxia.

(Fig. 2). Anoxic arrest for a period of 11 to 20 minutes significantly increased the chance of inotropic support ($p < 0.001$) and mortality ($p < 0.001$) as compared with anoxia for less than 10 minutes. However, spontaneous defibrillation occurred in more than 90 percent of

patients with anoxia up to 20 minutes, but after that length of time, electrical defibrillation was more frequently required ($p < 0.001$) with further increasing requirements of inotropic drugs ($p < 0.005$).

The use of induced ventricular fibrillation in anoxic arrest had a deleterious effect on the restoration of cardiac rhythm even with 20 minutes of anoxia ($p < 0.001$) and further deterioration of recovery was found beyond that time ($p < 0.005$) (Fig. 3).

The advantage of topical cooling was not clearly demonstrated although more than 65 percent of patients could be allowed to defibrillate spontaneously even for periods of longer than 41 minutes of anoxic arrest (Fig. 3).

In patients with relatively long anoxic arrest (more than 21 minutes), there was no significant difference in mortality rates between the group with 26° – 30°C body temperature and that with 31° – 35°C , but slight difference was noted when there was more than 41 minutes of anoxia (Table 4).

Variations in coronary perfusion technique were compared (Table 5). The mortality rate was significantly higher in patients in whom both coronary arteries were perfused ($p < 0.005$) and in those in whom perfusion was interrupted for more than 5 minutes ($p < 0.01$). High flow perfusion of more than 5 ml/kg/min tended to lead to a higher incidence of death, but this was not statistically significant ($p > 0.2$).

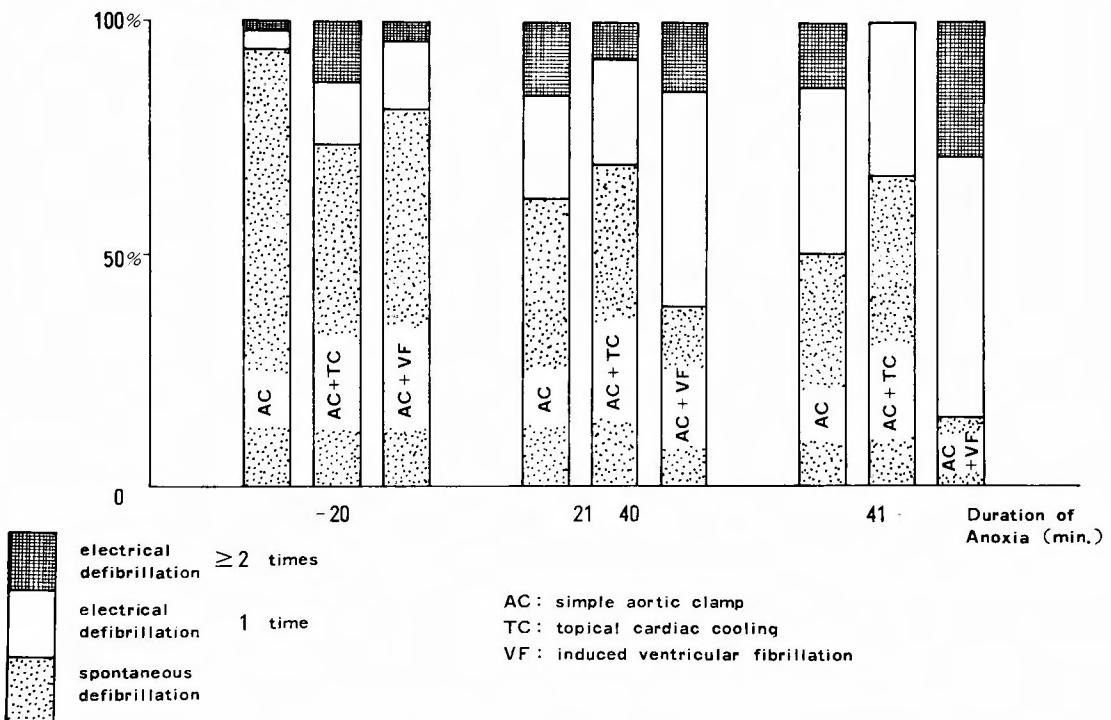


Fig. 3 Restoration of cardiac rhythm following anoxic arrest with or without topical cardiac cooling or electrical ventricular fibrillation.

Table 4 Mortality related to body temperature.

Anoxic Period (min.)	Total Case	Body Temperature (centigrade)	
		26° - 30°	31° - 35°
21 - 40	23/123 (18.7)	13/61 (21.3)	10/62 (16.1)
More than 41	4/29 (13.8)	1/13 (7.7)	3/16 (18.8)
Total	27/152 (17.8)	14/74 (18.9)	13/78 (16.7)

Early Death/Number of Case (Mortality)

Table 5 Mortality related to variation of coronary perfusion.

		Total Case	Perfusion Time	
			← 90 minutes	91 minutes →
Site of Perfusion	Left+Right	39/144(27.1)	22/ 81(27.2)	17/63(27.0)
	Left only	7/ 55(12.7)	4/ 37(10.8)	3/ 18(16.7)
Mode of Perfusion	Continuous	32/177(18.1)	14/102(13.7)	18/75(24.0)
	Intermittent	14/ 33(42.4)	11/ 25(44.0)	3/ 8(37.5)
Total Coronary Flow (ml/kg min.)	Less than 2.9	2/ 14(14.3)	1/ 12(8.3)	1/ 2(50.0)
	3.0—4.9	6/ 35(17.1)	3/ 16(18.8)	3/19(15.8)
	More than 5.0	30/111(27.0)	17/ 66(25.8)	13/45(28.9)

Early Death/Number of Case (Mortality)

Table 6 Mortality related to hemodilution.

Hemodilution (ml/kg)	Total Case	Perfusion Time (min.)	
		← 120	121 →
—20	$\frac{48}{467}$ (10.3%)	$\frac{28}{383}$ (7.3%)	$\frac{20}{74}$ (27%)
21—40	$\frac{176}{2147}$ (8.2%)	$\frac{69}{1799}$ (3.8%)	$\frac{107}{348}$ (30.7%)
41—	$\frac{135}{754}$ (17.9%)	$\frac{53}{543}$ (9.8%)	$\frac{82}{211}$ (38.9%)

Death/Number of Cases (Mortality)

Table 7 Mortality related to use of steroids.

	Total Case	Perfusion Time (min.)	
		← 120	121 →
Steroid	$\frac{219}{1479}$ (14.8%)	$\frac{69}{1081}$ (6.4%)	$\frac{150}{241}$ (37.7%)
No Steroid	$\frac{149}{1997}$ (7.5%)	$\frac{87}{1756}$ (5.0%)	$\frac{62}{241}$ (25.7%)

Death/Number of Case (Mortality)

The hemodilution was graded by the priming volume expressed as ml per kilogram of body weight. Moderate dilution (21-40ml/kg) was associated with the lowest mortality rate and marked dilution (more than 41ml/kg) with the highest mortality rate ($p < 0.001$) (Table 6).

The use of a corticosteroid, in a dose of 20-50 mg/kg of hydrocortisone, 2-3 mg/kg of methylprednisolone or 0.5-3.0 mg/kg of dexamethasone, did not provide any beneficial effect (Table 7). On the contrary, the mortality rate was unexpectedly high in the group treated with steroid, probably because of the frequent use of steroids in severe cases requiring longer cardiopulmonary bypass.

Discussion

There were significant differences in the mortality rates among the three groups. However, the comparison of these methods is not essential because the selection of the methods depends on the type of surgery in most circumstances. Therefore, an attempt was made to clarify the risk factors in each method.

Anoxic Arrest.....The safe period for normothermic anoxic arrest is generally considered to be 15-30 minutes⁽²⁾⁽⁷⁾⁽¹²⁾⁽²⁹⁾. Our results with simple anoxic arrest were almost the same. To increase the safe interval of anoxia, hypothermia which decreases metabolic requirements and hence reduces the relative need for oxygen has been introduced in the form of topical or systemic cooling. In our study, no significant difference in the effect of systemic hypothermia was found between body temperatures of 25°-30°C and 31°-35°C. This is probably because in most cases requiring anoxic arrest for more than 21 minutes, the body temperature was kept around 30°C and hence the temperature differences between the two groups were very slight.

The incidence of spontaneous defibrillation following anoxic arrest, which we consider to be a good indicator of the viability of the anoxic heart, showed no significant benefit of topical cooling, while spontaneous defibrillation occurred in about 70 percent of cases without relation to the duration of anoxia. The relatively poor recovery following a short anoxic arrest with topical cooling might be due to delayed rewarming of the cold myocardium. However, a steady recovery rate regardless of the length of the anoxic period indicated that the viability of the heart was well maintained by topical cooling for a long time.

Ventricular Fibrillation.....Although the deleterious effects of spontaneous or electrical ventricular fibrillation on hypertrophied left ventricle are well documented⁽⁴⁾⁽¹⁶⁾⁽²⁴⁾⁽²⁶⁾, the effect of electrical ventricular fibrillation on the nonhypertrophied heart is controversial. HOTTENROTT et al.⁽¹⁷⁻¹⁹⁾ demonstrated that during induced ventricular fibrillation, coronary flow was redistributed away from the left ventricle causing left ventricular ischemia in both hypertrophied and nonhypertrophied hearts. On the other hand, the safety of electrically induced ventricular fibrillation in the nonhypertrophied heart was shown by Cox et al.⁽¹⁰⁾ and WILSON et al.⁽³⁰⁾. Although in most of our cases the defect was congenital in origin and no distinction was made between hypertrophied and non-hypertrophied hearts, electrical ventricular

fibrillation without aortic clamping had no appreciable influence on the clinical results. However, electrical fibrillation combined with anoxic arrest had a significant adverse effect on the restoration of cardiac rhythm and, if continued for longer than 21 minutes, caused further deterioration.

Simple anoxic arrest and topical cardiac cooling can also produce ventricular fibrillation spontaneously, which is generally followed by cardiac standstill within 10 minutes after aortic occlusion. Therefore, electrical stimulation should be avoided or limited to as short a time as possible when anoxic or hypothermic arrest is used. HOTTENROTT et al.¹⁷⁾ reported that spontaneous fibrillation caused no adverse effect on the normal myocardium.

Coronary Perfusion.....Myocardial preservation is of greatest concern during surgery for aortic valve diseases, because the ventricle is hypertrophied and particularly vulnerable to ischemic injury. Although many surgeons prefer continuous and adequate coronary perfusion⁶⁾²²⁾²⁴⁾²⁸⁾, a number of complications are associated with selective coronary perfusion²⁵⁾²⁷⁾. Overperfusion of the coronary bed is one serious complication. Generally, coronary perfusion is controlled by flow rate and/or perfusion pressure. However, it seems difficult to predetermine the optimal pressure or flow rate for coronary perfusion because of a variety of conditions, such as the beating or fibrillating heart and various myocardial temperatures.

In our institutes, coronary perfusion was routinely controlled by keeping the perfusion pressure at around 120 mmHg. Hence, the flow rate varied with the resistance of the coronary bed. A high flow rate of more than 5 ml/kg/min (more than 250 ml/min) resulted in a higher mortality rate. ISOM et al.²⁰⁾ have suggested that a coronary flow of only 100-150 ml/min was theoretically adequate for myocardial oxygen consumption and that a flow rate greater than 300 ml/min might be damaging. COOLEY⁹⁾ stressed that there might be greater danger from overperfusion than from underperfusion. Therefore, it might be safe to use a loosely fitted coronary cannula to avoid excessive pressure and flow in coronary circulation, as pointed out by HIROSE et al.¹⁵⁾.

In some clinics, only the left coronary artery is perfused, while in others both coronary arteries are routinely perfused. The safety of perfusion of the left coronary alone has been questioned, for the right coronary artery is the major source of blood supply to the posterior wall of the left ventricle in some cases, especially in the type of right coronary preponderance which comprises approximately 40 percent of the hearts¹⁾. It is advisable, therefore, to perform coronary angiography preoperatively.

While we usually tried to perfuse both coronary arteries, perfusion of the right coronary artery was sometimes abandoned because of too small right coronary ostium or technical problems. Unexpectedly our study showed a higher mortality rate in cases with perfusion of both coronaries. The explanation of this finding remains unknown. However, the total flow rate when both coronary arteries were perfused exceeded 5 ml/kg/min in most instances, and this high flow might influence the results.

Effects of Hemodilution and Steroids.....Despite rheological benefits, the hazards of

extreme hemodilution have been pointed out by BUCKBERG et al⁵⁾. They showed experimentally that extreme hemodilution (less than 5 Gm hemoglobin) in normal hearts and moderate hemodilution (5-10 Gm hemoglobin) in hypertrophied hearts caused ischemia. The hemodilution in our study was graded by the amount of solution required for priming. Slight (less than 20 ml/kg), moderate (21-40 ml/kg) and severe (more than 41 ml/kg) hemodilution corresponded roughly to a hematocrit of more than 30, 25 and less than 20, respectively. With severe hemodilution the mortality rate was highest regardless of perfusion time.

Although the role of corticosteroid in myocardial protection has been reported²³⁾, we failed to demonstrate any benefit from this drug in our study. CODD et al.⁸⁾ found that methylprednisolone did not reduce the incidence of perioperative myocardial injury during coronary revascularization.

Recently, a number of cardioplegic and protective solutions have been introduced to increase the safe period of anoxic arrest and to avoid selective coronary perfusion. However, the efficacy of these solution is controversial³⁾¹¹⁾¹⁴⁾²¹⁾. Recently, we have used YOUNG's solution combined with glucose-insulin-potassium solution. This method provides effective protection even in hypertrophied hearts for as long as 90 minutes.

Summary

A total of 3568 patients who underwent open heart surgery during the past 12 years at Kyoto University Hospital and affiliated hospitals were retrospectively analyzed from the standpoint of myocardial protection. The methods of myocardial protection were assessed on the basis of 1) restoration of rhythmic contraction following anoxic arrest (spontaneous defibrillation), 2) inotropic support during and after bypass, 3) prolonged assisted circulation before weaning off bypass and 4) early death.

The following results were obtained :

- 1) The period of anoxia should be as short as possible, or limited to 20 minutes at the most.
- 2) Electrical ventricular fibrillation combined with anoxic arrest should be avoided, or limited to less than 20 minutes, if absolutely necessary.
- 3) Topical cardiac cooling might be effective to increase the safety of anoxic period, but we failed to demonstrate absolute benefit of this technique.
- 4) Special attention should be paid to the overperfusion of the coronary bed when selective coronary perfusion is required.
- 5) Severe hemodilution should be avoided.
- 6) No beneficial effect of steroids was demonstrated.

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和文抄録

開心術中の心筋保護の臨床的検討

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開心術中の心筋保護の良否は、それが術後成績を大きく左右するだけに、大きな関心事となっている。理論的に最良の心筋保護は、途絶することなく自然な状態で冠循環を維持することであろう。しかし、一方手術操作中、細部にわたり正確な病変の把握と修復を行なうため、冠循環を遮断して無血で静止した術野が必要とされる。心筋保護と術野改善対策の相反する2つの問題に対して従来種々の工夫が加えられ試みられてきた。

そこで我々は今回過去12年間に京大第2外科およびその関連病院で行なわれた開心術3500余例（超低体温法を除く）を心筋保護の観点より分析を行なった。

手術手技は大別すると、大動脈非遮断、大動脈遮断および選択的冠灌流に分けられ、更にこれらに併用して心局所冷却および電気的心室細動が使用された。

これらの手技の評価は、早期死亡、術中術後の強心剤使用の有無、体外循環離脱の難易および阻血後の心

拍動再開（電気的除細動の必要性）など臨床的見地より行なわれた。

その結果は以下の如くである。

(1) 大動脈遮断は出来るだけ短時間であることが好ましく、長くとも20分以内とすべきである。

(2) 電気的心室細動の使用は阻血心に対しては使用すべきでなく、どうしても必要なときでも20分以内に制限すべきである。

(3) 局所冷却法は長時間の阻血を必要とする場合は有効と考えられるが、今回は決定的有意差を見い出せなかった。

(4) 選択的冠灌流を行なう場合、overperfusionに留意する必要がある。

(5) 過度の血液稀釈は避けるべきである。

(6) 術中のステロイド使用の効果は明らかではなかった。