Department of Cardiovascular Surgery

Kazuhiro Hashimoto, *Professor*
Yoshimasa Sakamoto, *Associate Professor*
Yuzuru Nakamura, *Associate Professor*
Kei Tanaka, *Assistant Professor*
Ryuichi Nagahori, *Asssitant Professor*
Kiyozo Morita, *Professor*
Kouji Kawahito, *Associate Professor*
Tatsuumi Sasaki, *Associate Professor*
Kouji Nomura, *Assistant Professor*
Yoshimasa Uno, *Assistant Professor*

General Summary

The main investigation in our department involved clinical study, evaluation of alterations in cardiac performance and long-term results after corrective surgery, and experimental studies to solve theclinical problems we are facing. Clinical investigations, including follow-up studies, of valvular and ischemic heart diseases were a main area of our clinical research, as were studies of complex congenital anomalies. The recent increase in aortic aneurysms has become another concern in our field. Starting this year we have examined mid-term results, because we had a large enough number of surgical cases in the last few years. New treatment approaches utilizing new surgical techniques, new devices, and research outcomes have been investigated and attempted. We are also performing several experimental studies with in vivo models. The experimental projects include protection of the lung during extracorporeal circulation and postischemic conditioning after cardiac arrest. Our studies were completed and submitted to journals. The major activities are described below.

Research Activities

Basic research

1. Studies of cardiopulmonary protection strategies during open-heart surgery

1) Experimental studies on the prevention of ischemia-reperfusion-induced pulmonary dysfunction after cardiopulmonary bypass with terminal leukocyte-depleted lung reperfusion

Background: We tested the hypothesis that ischemia-reperfusion-induced pulmonary dysfunction after total cardiopulmonary bypass (CPB) is prevented by controlled pulmonary reperfusion with leukocyte-depleted venous (hypoxemic) blood during the early phase of reperfusion.

Methods: Twenty-one, 4- to 5-week-old piglets underwent 180 minutes of total CPB with occlusion of the pulmonary artery (PA) followed by reperfusion. In group I, unconditioned reperfusion was performedby means of simple unclamping of the PA, whereas selective pulmonary reperfusion with either leukocyte-depleted arterial (hyperoxemic) blood (in group II) or venous (hypoxemic) blood (in group III) was applied for 15 minutes at a flow rate of 10 mL/kg/minute before PA unclamping.

Results: Uncontrolled reperfusion in group I caused pulmonary dysfunction, characterized by increased alveolar-arterial oxygen tension difference and decreased static lung compliance and pulmonary vasoconstriction, associated with increases in lung myeloper-

oxidase and interleukin 6 levels and endothelin 1 washout after reperfusion.
Terminal leukocyte-depleted lung reperfusion significantly decreased post-CPB lung dysfunction and vasoconstriction, if hypoxemic blood was used as the reperfusate. In contrast, the benefit of terminal leukocyte-depleted lung reperfusion against post-CPB lung dysfunction was nullified by the use of hyperoxemic blood.
Conclusions: Leukocyte-depleted reperfusion with hypoxemic blood protects against ischemia-reperfusion-induced pulmonary dysfunction by limiting endothelial damage, cytokine release, and leukocyte activation.
2) Effect of postconditioning: Experimental study using an in vivo piglet model for the cardiovascular surgical setting on the reversal of myocardial stunning by ischemic postconditioning
Background: This study tested the hypothesis that ischemia/reperfusion-induced myocardial damage can be reduced by postconditioning at reperfusion.
Methods: Eighteen piglets underwent 90 minutes of ischemia followed by 60 minutes of reperfusion on CPB. In 12 piglets, ischemic postconditioning strategies were applied before aortic unclamping: either 6 cycles of 10-second ischemia/reperfusion or 3 cycles of 30-second ischemia/reperfusion. The other 6 piglets were not treated (control).
Results: Left ventricular systolic and diastolic dysfunction, associated with oxidant-induced biochemical injury, was noted in the control group. In contrast, postconditioning allowed significantly better functional recovery of the left ventricle and less myocardial biochemical injury.
Conclusion: Ischemic postconditioningduring the early phase of reperfusion produced prompt myocardial functional recovery with decreased biochemical injury in a piglet model of CPB.

Clinical Studies of Pediatric Heart Surgeries
1. Coagulability and fibrinolytic function in Fontan circulation
We have measured plasma levels of thrombin-antithrombin-3 complex (TAT) as an index of coagulability and α2-plasmin inhibitor-plasmin complex (PIC) as an index of fibrinolytic function in 20 patients subjected to extracardiac Fontan circulation (mean age at operation, 4.2 years). The levels of both TAT and PIC remained higher than normal for 6 months after surgery, even when warfarin was administered. However, levels then began to gradually decrease and had almost completely normalized by 12 months after surgery. This study suggests that patients might need warfarin as anticoagulation therapy for the first year after Fontan circulation, because of the activated state of coagulability. However, warfarin could be replaced by an antiplatelet agent in patients who show normal results and have no major complications for 12 months after surgery.
2. Intraoperative evaluation of pulmonary flow reserve capacity and a new method to predict post-Fontan hemodynamic status
In 12 patients in whom the staged Fontan procedure was indicated after the bidirectional Glenn procedure, we measured superior vena cava flow,which is equivalent to PA flow in bidirectional Glenn physiology, by means of a transit-flow meter intraoperatively.The measurement of PA flow and pulmonary vascular reserve (PVR), incorporated with

serial volume loading, allowed the assessment of PVR capacity in response to an increase in pulmonary flow to simulate Fontan circulation. The PVR capacity, assessed by the percent reduction of pulmonary resistance in response to increased pulmonary flow, was revealed to be a strong indicator of the post-Fontan outcome and the final central venous pressure (CVP) at Fontan circulation. In 8 patients who underwent the Fontan operation, there was a significant relationship between the actual CVP and the CVP predicted by means of intraoperative simulation.

3. Surgical outcomes and long-term results of the Ross operation: Effect of autograft dilatation

Surgical outcomes and long-term results of the Ross operation were reviewed in 35 patients who underwent the Ross procedure from 1995 through 2008. Autograft function was assessed by periodic echocardiographic evaluation postoperatively for up to 14 years. There was no operative or acute deaths or late reoperation for autograft regurgitation: (rate of freedom from reoperation for autograft failure: 87% at 14 years). Excellent durability of the implanted pulmonary autograft valve was noted, especially in pediatric patients and patients with preoperative aortic stenosis.

Clinical study of adult cardiac surgery

1. Valve disease

1) Reconstruction surgery for complex degenerative mitral valve disease

Limitations and long-term results of the surgical method, based on excess leaflet resection

The basic concept of our approach for the complex degenerative mitral valve disease is to create a smooth clear zone and coaptation surface by removing the excess prolapsed leaflet. In addition to leaflet resection, annular remodeling, which can be achieved with the complete ring, contributes to physiological reconstruction of the mitral valve regardless of the location or area of the diseased prolapsing leaflet. In the case of a wide anterior prolapsed area, leaflet resection with artificial chordae is recommended. Simple and complex prolapse cases did not differ in long-term results.

2) Midterm results with the 19-mm Carpentier-Edwards pericardial bioprosthesis in the aortic position

We have usually used Carpentier-Edwards aortic pericardial valves in patients 65 years or older according to published guidelines. In patients with a small aortic annulus, either annular enlargement or insertion of new-generation prosthetic valves has been proposed to minimize the postoperative residual transprosthetic gradient. Annulus enlargement must be performed in a small percentage of elderly patients with an extremely small annulus if the smallest-sized mechanical or tissue valve can be inserted anatomically. Excellent results have been achieved with bovine pericardial valves in the aortic position both with 19-mm valves and with larger valves. We are comfortable using the 19-mm bovine pericardial valves for elderly Japanese patients

2. Ischemic heart disease

1) Training of bypass surgeons in off-pump coronary artery bypass graft generation

This is the transitional stage from the conventional on-pump coronary artery bypass grafting (CABG) generation to the off-pump generation. In this situation, many teaching hospitals have their own systems for training resident physicians who are not

fully experienced with conventional CABG. We can train resident physicians with the desk model system and simple operative devices for off-pump CABG.

3. Thoracic aneurysm

1) A safe and simple method of retrograde cerebral perfusion

Although methods of brain protection in aortic aneurysm surgery have already been established, strokes and air embolism after cannulation into the atheromanous aortic arch branches still occur. Such complications could be avoided with retrospective cerebral perfusion at the beginning of circulatory arrest. We have performed cardiopulmonary bypass using ascending aortic and right atrial cannulation with a rectal temperature of 25°C. After the ascending aorta is clamped, cardiac arrest is achieved with anantegradecardioplegic solution. Retrograde cerebral perfusion begins through the cannula for retrograde cardioplegia via the superior vena cava (200–250 ml/minute) to remove debris or air. This simple method is beneficial for brain protection.

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