

Department of Cardiovascular Surgery

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General Summary

The main research activities in our department involved clinical study, evaluation of alterations in cardiac performance and long-term results after corrective surgery, and experimental studies to solve the clinical 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. We have examined short-term and mid-term results and confirmed their excellence. Other fields of cardiac surgery were also analyzed and found to have yielded excellent results as well. We are also continuously performing several experimental studies with *in vivo* models. The experimental projects include protection of the heart during cardiac arrest and pulmonary valve function. The major activities are described below.

Research Activities

Experimental studies of congenital heart diseases: The effect of cardiopulmonary factors on the severity of pulmonary regurgitation in an acute swine model

The progression of pulmonary regurgitation after intracardiac repair for congenital heart defects requiring right ventricular (RV) outflow tract reconstruction results in the RV volume overload and subsequent RV dysfunction, contributing to poor morbidity and reoperation. We examined the effects of cardiopulmonary factors (RV systolic function [end-systolic elastance, E_{es}] and pulmonary vascular resistance index [PVRI]) on the severity of pulmonary regurgitation (PR) in an acute swine cardiopulmonary bypass (CPB) model. In 8 pigs (body weight, 14 ± 2 kg), an acute PR model was established with the use of CPB. The severity of PR (%PR) assessed with a Doppler flow meter (backward/forward flow area) was $40\% \pm 4\%$ at the steady state after the operation. During the serial alterations of PVRI by manipulation of ventilation and NO inhalation, %PR increased in parallel with PVRI ($p < 0.01$ %PR versus PVRI). Furthermore, %PR was reduced by stepwise increases in RV E_{es} by dobutamine infusion. In conclusion, the hemodynamic effect of PR depends on the patient's cardiopulmonary status (i.e., RV function and pulmonary vasoconstriction) in addition to the status of pulmonary valve competence.

Experimental studies of new therapeutic strategies of cardiopulmonary protection during open-heart surgery

1. Reversal of oxidant-mediated biochemical injury and prompt functional recovery after prolonged single-dose crystalloid cardioplegic arrest in immature piglet heart by the terminal warm-blood cardioplegia supplemented with a phosphodiesterase III inhibitor
Terminal blood cardioplegia (TWBCP) alone provides insufficient benefits after prolonged ischemia and is associated with inevitable oxidant-mediated injury. To examine methods of avoiding oxidant-mediated myocardial reperfusion injury and of facilitating prompt functional recovery, we examined the effects of TWBCP supplemented with high-dose olprinone, a phosphodiesterase III inhibitor, which has the potential to reduce oxidant stress and calcium overload, after prolonged single-dose crystalloid cardioplegic arrest in a model of CPB in immature piglets. Fifteen piglets were subjected to 90 minutes of cardioplegic arrest on CPB, followed by 30 minutes of reperfusion. In group I, uncontrolled reperfusion was applied without receiving TWBCP; in group II, TWBCP was given; and in group III, TWBCP was supplemented with olprinone (3 µg/ml). Group III showed significant left ventricular (LV) performance recovery (Group I, 26.5%±5.1%; group II, 42.9%±10.8%; group III, 81.9%±24.5%, $p < 0.01$ versus groups I and II), associated with significant reduction of troponin T and lipid peroxidation at the reperfusion phase. In groups III no piglets required electrical cardioversion. On the basis of this study, we conclude that TWBCP with olprinone reduces myocardial reperfusion injury by reducing oxidant-mediated lipid peroxidation and accelerates prompt and persistent LV functional recovery while suppressing reperfusion arrhythmia.

2. Effect of postconditioning: Experimental study using a piglet model of cardiovascular surgery on the reversal of myocardial stunning by ischemic postconditioning

Background: This study tested the hypothesis that myocardial damage induced by ischemia/reperfusion can be reduced by postconditioning at reperfusion.

Methods: Eighteen piglets were subjected to 90 minutes of ischemia followed by 60 minutes of reperfusion on CPB. In 12 of them, ischemic postconditioning strategies (6 cycles of 10 seconds of ischemia/reperfusion or 3 cycles of 30 seconds of ischemia/reperfusion) were applied before aortic unclamping, whereas the other 6 were not treated (control).

Results: In the LV, both systolic and diastolic dysfunction, associated with oxidant-induced biochemical injury, were noted in the control group. In contrast, postconditioning resulted in significantly better LV functional recovery and less myocardial biochemical injury.

Conclusion: Ischemic postconditioning during the early phase of reperfusion produces prompt myocardial functional recovery and inhibits biochemical injury in a piglet model of CPB.

Clinical studies of pediatric heart surgeries

1. Effects of oral pulmonary vasodilators (sildenafil and bosentan) in high-risk candidates for the Fontan procedure after the bidirectional Glenn operation

We have retrospectively analyzed the effects of treatment with oral pulmonary vasodilators (sildenafil and bosentan) on the hemodynamic risk profile (pulmonary arterial pres-

sure [PAP], pulmonary vascular resistance: pulmonary resistance [Rp] and PA index) in 8 high-risk candidates for the Fontan procedure and 10 untreated control patients.

In the treatment group, 8 patients who underwent bidirectional Glenn (BDG) operation, significant reductions in Rp and PAP were noted 6 and 12 months after the operation, whereas no changes were demonstrated in the control group. This study suggests that treatment with oral pulmonary vasodilators (sildenafil and bosentan) can reduce pulmonary risk factors in candidates for the Fontan procedure.

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 BDG operation, we measured superior vena cava flow, which is equivalent to PA flow in BDG physiology, by means of a transit-flow meter intraoperatively. Measurement of PA flow and pulmonary vascular resistance, incorporated with serial volume loading, allows pulmonary vascular reserve capacity to be assessed in response to an increase in pulmonary flow to simulate Fontan circulation. The pulmonary vascular reserve capacity, assessed by the percent reduction in Rp in response to increased pulmonary flow, was revealed to be a strong indicator of post-Fontan outcome and a final central venous pressure (CVP) with Fontan circulation. In 8 patients who had undergone the Fontan procedure, there was significant relationship between the actual CVP and the CVP predicted by means of intraoperative simulation.

3. The surgical outcome and long-term results of the Ross operation: Effect of autograft dilatation

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

Clinical study of adult cardiac surgery

1. Valve disease

1) Surgical intervention for active mitral infectious endocarditis

Mitral valve repair has been performed even when the leaflets have been severely damaged by active mitral infectious endocarditis. Recently, our basic approach to active mitral infectious endocarditis is to perform surgery early in the active phase while antibiotics are administered, with the aim of improving the rates of cure and of successful mitral valve repair. It is possible to remove vegetations and the infected parts of leaflets and to suture directly or use patch plasty if the infection has not reached the annulus. There are many sources of patch materials which are treated with glutaraldehyde. We are using the Xenomedica patch (Baxter Healthcare Corp., Horw, Switzerland) because of the ease of handling.

2) Mitral valve reconstruction

Leaflet resection for posterior leaflet prolapse has been a standard repair procedure with

good long-term durability. Both quadrangular and triangular leaflet resections tend to cause posterior displacement of the coaptation point, but coaptation line was satisfactory in terms of leaflet geometry. The mobility of the resected leaflet was preserved, and the anterior leaflet could move to coapt with the resected posterior leaflet. Echocardiography revealed excellent mobility of the resected posterior leaflet. Resection procedures have been successfully used to repair mitral valves affected by myxomatous degeneration.

3) Assessment of our mitral valve repair without systolic anterior motion

We have never encountered systolic anterior motion requiring treatment after mitral valve repair. The key for avoiding systolic anterior motion after mitral valve repair is to resect an excess amount of prolapsed leaflet to obtain a smooth coaptation line, as in single anterior leaflet closure, and to select an appropriately sized ring.

4) Aortic valve replacement

Patient age is an important factor in the choice of valves to replace the aortic valve. The first choice in patients older than 65 years has been a bioprosthetic valve, but such valves are increasingly used for patients younger than 65 years. Long-term results have been satisfactory for both mechanical and bioprosthetic valves. The frequency of bioprosthetic valve use has increased, but only for patients aged 55 to 60 years. In elderly patients the use of mechanical prostheses has been limited to patients with a narrow aortic annulus.

2. Ischemic heart disease

1) Increasing of coronary artery bypass grafting for patients with hemodialysis and the construction of multiple intensive care units

The percentage of patients receiving hemodialysis who undergo coronary artery bypass grafting (CABG) has rapidly increased (2007, 5.1%; 2008, 7.7%; 2009, 12.4%; 2010, 25.0%). The risk of CABG for patients receiving hemodialysis is high, and the postoperative management of these patients may present difficult challenges to the cardiac surgical team. At our institution, specialists from many fields, including nephrology and infection control, participate in the postoperative care of patients in the intensive care unit. This team approach has helped shorten the duration of patients' stays in the intensive care unit, even as the percentage of patients receiving hemodialysis has increased.

2) Training of surgeons in the transitional stage from conventional CABG to off-pump CABG

The procedure of CABG has changed dramatically in the past 10 years from conventional CABG with CPB to CABG without CPB. In our teaching hospital, it would be possible to train resident physicians with the desk-training model system, simple devices, and various anesthetic methods and to achieve satisfactory results.

3. Thoracic aneurysm

1) Preventing cerebrovascular complications in aortic arch replacement

The first choice for an aortic infusion line is an ascending aorta without calcification. If there is porcelain or arteriosclerosis, we select an axillary artery. Moreover, we have cannulated atheromatous branches of the aortic arch which have sufficient backflow, achieved by means of selective cerebral perfusion, followed by initial retrograde cerebral perfusion. To prevent the complications of cerebral infarction and air embolism, retro-

grade cerebral perfusion is a safe and simple method of brain protection.

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