

Department of Cardiovascular Surgery

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General Summary

The main investigations in our department involved clinical studies, evaluation of alterations in cardiac performance, and long-term results after any type of cardiac surgery, and animal experimental studies to address current clinical problems. Clinical investigations, including introduction of new techniques and follow-up studies, of valvular and ischemic heart diseases were a main area of our clinical research, as were studies of complex congenital anomalies. A recent topic in adult surgery is the introduction of a new field — transcatheter aortic valve replacement — and we started preparing to perform such operations. The recent increase in aortic aneurysms has continued, and a surgical strategy has been established and has achieved good results. These good results are apparently related to collaboration with the Division of Vascular Surgery. We are also performing several experimental studies with *in vivo* models. Our experimental projects include protection of the heart during cardiac arrest and pulmonary valve function. The major activities are described below.

Research Activities

Clinical investigation of myocardial protection during pediatric heart surgery

In infants with ventricular septal defect, atrioventricular septal defect, or other congenital malformations who underwent open-heart surgery with various cardioplegic strategies, biochemical markers for myocardial injury (troponin T) and oxidative stress (8-iso-prostane) were measured intraoperatively. This retrospective study confirmed the benefits of terminal warm-blood cardioplegia for preventing reperfusion-induced biochemical injury.

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

1. Effect of ischemic postconditioning and remote preconditioning: Experimental study in an *in vivo* piglet model of the reversal of myocardial stunning by ischemic postconditioning and remote preconditioning

This study tested the hypothesis that ischemia/reperfusion-induced myocardial damage can be reduced by postconditioning at reperfusion. Eighteen piglets underwent 90 minutes of ischemia followed by 60 minutes of reperfusion on cardiopulmonary bypass. In 12 of them, ischemic postconditioning strategies — 6 cycles of 10-second ischemia/reperfusion (PC-I) or 3 cycles of 30-second I/R (PC-II) — were applied before aortic unclamping, whereas the other 6 were not treated (control). Left ventricular (LV) sys-

tolic and diastolic dysfunction associated with oxidant-induced biochemical injuries were noted in the control group. In contrast, postconditioning led to significantly better LV functional recovery and less myocardial biochemical injury. On the basis of this study we concluded that ischemic postconditioning at the early phase of reperfusion produces prompt myocardial functional recovery with less biochemical injury in a piglet model of cardiopulmonary bypass. Furthermore, to develop clinically applicable strategies of conditioning after myocardial ischemia, we tested the efficacy of “remote” conditioning by means of ischemia-reperfusion of the abdominal aorta just before myocardial reperfusion.

Clinical studies of pediatric heart surgeries

1. Postoperative changes in coagulability and fibrinolytic function in Fontan circulation: Possibility of the conversion of anticoagulation therapy

There is still no consensus concerning the postoperative use and duration of anticoagulation therapy with warfarin for patients with Fontan circulation. We evaluated changes in coagulability and fibrinolytic function after surgery and tried to use these changes as indicators for anticoagulation therapy. Plasma levels of thrombin-antithrombin 3 complex (TAT) as an index of coagulability and levels of α 2-plasmin inhibitor-plasmin complex (PIC) as an index of fibrinolytic function were measured in 16 patients with extracardiac Fontan circulation (mean age at operation, 4.2 years). The levels of both TAT and PIC remained higher than normal within 6 months after surgery, even in patients receiving warfarin. The levels of both TAT and PIC began to gradually decline and had almost normalized by 12 months. Confirming these results, we have changed from warfarin to antiplatelet agents for such patients. Even after this change, plasma levels of TAT and PIC have remained normal, and no patients had evidence of thromboembolic events on echocardiography. This study suggests that patients with Fontan circulation require anticoagulation therapy with warfarin for the first postoperative year, because of activated coagulability. However, warfarin can be replaced with an antiplatelet agent for patients with normal levels of TAT and PIC and no major complications more than 12 months after surgery.

2. 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 effect of treatment with oral pulmonary vasodilators (sildenafil and bosentan) on the hemodynamic risk profile (pulmonary arterial pressure and pulmonary vascular resistance) in 8 high-risk candidates for the Fontan procedure and in 10 control patients not treated with oral pulmonary vasodilators. In the 8 patients who received oral pulmonary vasodilators, significant reductions in pulmonary vascular resistance and pulmonary arterial pressure were noted 6 and 12 months after the bidirectional Glenn operation, whereas no changes were seen in the control group. This study suggests that treatment with oral pulmonary vasodilators (sildenafil and bosentan) improves pulmonary risk factors in candidates for the Fontan procedure.

3. Surgical outcomes 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 from 1995 through 2008. Autograft function was assessed postoperatively with periodic echocardiographic examinations for up to 14 years. There were no operative or acute deaths or late reoperation for patients with regurgitation after receiving autografts. The rate of freedom from reoperation for autograft failure was 87% over 14 years. The implanted pulmonary autograft valve showed excellent durability, especially in pediatric patients and patients with preoperative aortic stenosis.

Clinical study of adult cardiac surgery

1. Therapeutic strategy for patients older than 80 years with aortic stenosis in the transcatheter aortic valve implantation generation

Reflecting the recent aging society, nearly 10% of valve operations are performed in elderly, high-risk patients who are candidates for transcatheter aortic valve implantation. The operative risk is approximately 5%, and the surgical outcomes of aortic valve replacements have been satisfactory. There have been no patients for whom cardiopulmonary bypass was contraindicated and no serious perioperative complications. At present, surgical indications should be decided on the basis of the preoperative condition, risk scores, and other factors.

2. Choice of surgical procedures according to cause of degenerative mitral valve regurgitation: From Barlow's disease to fibroelastic deficiency

Surgical strategies should be devised on the basis of the cause of degenerative mitral valve regurgitation, from Barlow's disease, the incomplete type, and the fibroelastic deficiencies. The surgical technique of triangular resection is adapted to anterior leaflet prolapse, and the area of resection is limited as much as possible to the rough zone. Artificial chordal reconstruction is used in addition to leaflet resection if the prolapsed area is wide. In the posterior prolapse, the triangular resection is adapted, and the defect is closed with simple sutures. The diseased prolapsed area between the healthy supported chordae is removed, but the annular lesion should not be cut. The commissural small prolapse can be corrected with an edge-to-edge procedure, and the resection and suture procedure should be adapted to the larger commissural prolapse. In most cases, the flexible saddle rings are sutured for the annuloplasty. If the posterior leaflet height is supposed to be long, partial rings may be suitable for avoiding systolic anterior movement. The ring size is decided on the basis of the surface of the anterior leaflet and the distance between the anterior and the posterior fibrous triangles. Eighty percent of our cases were of the fibroelastic deficiency type, which can be repaired with quadrangular or triangular resection alone without sliding techniques. The resection and suture surgical techniques for removing the diseased prolapsed areas are beneficial for avoiding the recurrence of regurgitation, but there is still an increased tendency for reoperation in cases, such as cases of Barlow's disease, with anterior wide prolapse. We must select more suitable and effective procedures for each case.

3. Heart team: The role of the perioperative heart team, composed of the intensive care unit physicians and rehabilitation staff, in dealing with patients receiving hemodialysis who underwent coronary artery bypass graft surgery

Recently, the number of patients who are receiving hemodialysis and undergo coronary artery bypass graft surgery has increased. However, the operative and morbidity risks in

patients receiving hemodialysis are high. At our institution, interdisciplinary heart teams have contributed to excellent operative outcomes. The perioperative management of patients has been decided by the heart team after daily discussions of treatment plans. Total perioperative care in the intensive care unit has helped relieve the burden on the general wards.

4. Thoracic aneurysm surgery: Preventing cerebrovascular complications in aortic arch replacement surgery

The first choice of an aortic infusion line is an ascending aorta without calcification. If the condition of the aorta is unsatisfactory, we select an axillary artery for aortic infusion. However, because this infusion is insufficient for preventing cerebral infarction during surgery, we also cannulate the atheromatous arch branch vessels under sufficient backflow that can be achieved with selective cerebral perfusion, following initial retrograde cerebral perfusion with a flow rate of 300 ml/minute for several minutes. To prevent operative cerebral infarction and air embolism, retrograde cerebral perfusion is a beneficial, safe, and simple procedure for brain protection.

5. Management of postoperative infections: New problems and steps concerning postoperative mediastinitis

The increasing numbers of patients with diabetes or chronic kidney dysfunction has increased the number of patients at high risk for surgical site infection (SSI). Such SSIs are a heavy burden for both patients and hospitals. Our basic strategies to prevent SSI are as follows: 1) check the nasal cavity, 2) have the patient take a shower, 3) shave the patient in the operating room, 4) sterilize the body surface with benzyl chloride alcohol and iodine, 5) infuse antibiotics (cephazolin) every 3 hours during the operation and continue 3 times a day for 4 days after the operation, 6) use double-layered gloves and change every 3 hours during the operation, 7) thoroughly irrigate the surgical incision with water and use absorbable monofilament sutures and single stitching if possible, 8) control the blood glucose level with continuous infusion of insulin, 9) routine postoperative control by the infection-control team and the dental team, and 10) early postoperative rehabilitation by physical therapists. This method of postoperative management has decreased the postoperative complication of mediastinitis. Recently, a new type of postoperative SSI, which appears after discharge in patients with diabetes mellitus who are unaware of the disease or live alone, has become more frequent. For these patients, it is also important to intensify close preoperative surveillance and educate them regarding the management of the surgical wound and sanitary conditions after discharge. These efforts have led to good results.

Publications

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