Department of Surgery Division of Pediatric Surgery and Vascular Surgery

Takao Ohki, Professor and Chairperson Hitoshi Sakuda, Assistant Professor Naoki Toya, Assistant Professor Atsushi Ishida, Assistant Professor Yuji Kanaoka, Assistant Professor Joji Yoshizawa, Assistant Professor

General Summary

Pediatric Surgery

The Division of Pediatric Surgery at The Jikei University Hospital is dedicated to providing expert surgical care for fetuses, infants, children, and adolescents with congenital and acquired conditions. Our surgeons remain committed to the ongoing development of new surgical techniques for treating diseases in children, particularly minimally invasive approaches to replace more invasive open procedures that require large incisions.

Vascular Surgery

Research projects of our department have focused on the development of the endovascular repair of aneurysms, treatment of peripheral arterial disease with drug-eluting stents, and clinical studies of specific antibodies for heparin-platelet factor 4 (PF4) complexes.

Research Activities

Pediatric Surgery

1. Education

Education for medical students: The patients undergoing pediatric surgery often have congenital anomalies. For this reason, lectures on pediatric surgery for medical students are based on embryology.

Education for physician training : Three objectives for physician training in pediatric surgery are: 1) how to obtain a blood samples from pediatric patients, 2) understanding fluid therapy for pediatric patients, and 3) learning the technique of buried sutures.

Education for surgical residents: They are able to serve as operators or assistants for pediatric surgery.

- 2. Clinical studies
- 1) Manometry for children with constipation
- 2) Testosterone injection for micropenis
- 3) Endoscopic treatment using Deflux, a hyaluronic acid/dextranomer gel (Q-Med AB, Uppsala, Sweden) for grades IV and V vesicoureteral reflux
- 4) Development of introducers for central venous access

5) In cases of severe gastroesophageal reflux, a surgical procedure called fundoplication is performed. This procedure is performed laparoscopically in our hospital. With minimally invasive laparoscopic surgery, pain is minimized, and recovery after surgery is faster. The number of neurologically handicapped children with gastroesophageal reflux has been increasing in our hospital. Carbon oxide changes the balance of electrolytes and acid-base in laparoscopic surgery.

6) The Nuss procedure aims to force the sternum forward and hold it there with an implanted steel bar, but without making a large incision to resect the abnormal cartilage. In this procedure, the curved steel bar is placed under the sternum through 2 small incisions on the sides of the chest. The number of patients with pectus excavatum treated surgically at The Jikei University Hospital is the third highest in Japan.

7) Molecularly targeted therapy using an antiangiogenic factor

8) Extracorporeal ultrafiltration for septic shock using a rat model

During sepsis, microorganisms release various endotoxins, including such cytokines as tumor necrosis factor alpha and interleukin 6 and complement components, that activate cascade systems to a greater or lesser extent. Plasmapheresis is used to remove these factors. We created a rat model of sepsis and evaluated the effects of plasmapheresis.

9) New diagnostic and therapeutic methods for neuroblastoma

A problem for nursing students is that they have no lectures related to pediatric surgery. A problem for fifth-year medical students is that there is no bedside teaching about pediatric surgery. The curriculum should, therefore, be changed.

Vascular Surgery

1. Development of endovascular repair of thoracoabdominal aneurysms

Although stent grafts for the treatment of abdominal aortic aneurysms (AAAs) have been developed and are commercially available, no such stent grafts are available for the treatment of thoracoabdominal aortic aneurysms (TAAAs). The surgical death rate following open surgery for the treatment of AAAs is satisfactory, but that for TAAAs remains unacceptably high at 15% to 20%, and further improvement is desperately needed. Because a TAAA involves 1 or more visceral arteries, visceral perfusion must be maintained while the aneurysm is excluded with stent grafts. We have used a custom-made branched stent graft in combination with covered stents (for visceral reconstruction) for the treatment of TAAAs that were considered inoperable because of comorbid conditions or a hostile thorax/abdomen. Although stent graft repair for TAAAs requires long operative and fluoroscopic times, this treatment is feasible and safe.

2. Development of endovascular repair of aortic arch aneurysms: Retrograde *in-situ* branched surgery

We have developed a new minimally invasive operation for aortic arch aneurysms. After carotid-carotid bypass surgery is performed and stent grafts are placed, a needle is used to push the stent graft thorough one side of a carotid artery, after which a covered stent is inserted as a branch and deployed into the stent graft (in an *in-situ* retrograde fashion). We have examined this retrograde *in-situ* branched surgery in an *in-vitro* study and have applied it clinically. This operation is expected to be a less invasive surgery for aortic arch aneurysms.

3. Research on drug-eluting stent in the superficial femoral artery

The Zilver PTX drug-eluting peripheral stent (Cook Medical, Bloomington, IN, USA) is specifically designed and approved to treat peripheral arterial disease affecting the superficial femoral artery, the main vessel of the thigh. The Zilver PTX is a self-expanding

stent made of nitinol, a space-age "shape memory" metal that offers unique mechanical advantages for a stent in the superficial femoral artery.

Both a global registry and a randomized controlled trial, in which most patients were enrolled in the United States, but also in Germany and Japan, is awaiting its 1-year primary endpoint, which should be reached in August 2009. We are participating in this trial.

4. Clinical study of specific antibody for heparin-PF4 complexes

Heparin is commonly used for anticoagulation in vascular surgery. Heparin-induced thrombocytopenia (HIT) is a rare but life-threatening complication with thrombosis of veins and arteries. Even if heparin use is limited, it occasionally induces the production of specific antibodies against heparin-PF4 complexes. Patients with such antibodies are at increased risk for HIT. The prevalence of these antibodies in patients receiving heparin is presumably underestimated. Accordingly, we prospectively measured antibodies against heparin-PF4 complexes and activity of PF4 and investigated whether they are related to symptoms of HIT, particularly in patients undergoing major vascular surgery. We measured these variables in 300 patients for 2 years.

The percentage of patients with antibodies to heparin-PF4 complexes was approximately 13%, which was higher than expected. Moreover, PF4 activity tended to be higher in antibody-positive patients than in antibody-negative patients. The results of this study are being statistically analyzed and will be reported in 2009.

5. Research on prevention of reperfusion injury during endovascular aneurysmal repair. Large sheaths are usually chosen for endovascular aneurysmal repair. If the inserted sheath is retained at the femoral artery for a long time, the ischemic time of the lower extremities becomes longer, and reperfusion syndrome might occur. We have used a small sheath to supply blood flow to the distal lower extremities and to prevent complete ischemia of the lower extremities and consequent reperfusion syndrome.

Publications

Ohki T. EVAR takes root in Japan. *Endovascular Today* 2010; **9:** 46-8.

Ohki T. Cordis incraft system studied in INNO-VATION. *Endovascular Today* 2010; **9:** 14.

Ohki T. Terumo's Misago stent to be studied in US and Japan. *Endovascular Today* 2010; **9**: 22. **Shigematsu H, Nishibe T, Obitsu Y, Matsuzaki K, Ishida A, Miyata T, Shindo S, Hida K, Ohta T, Ando M, Kawasaki T, Yasugi T, Matsumoto T.** Three-year cardiovascular events and disease progress in patients with peripheral arterial disease: results from the Japan Medication Therapy for Peripheral Arterial Disease (J-METHOD). *Int Angiol* 2010; **29(2 Suppl):** 2–13.

Kanaoka Y, Inagaki E, Hamanaka S, Masaki H, Tanemoto K. Analysis of reactive oxygen metabolites (ROMs) after cardiovascular surgery as a marker of oxidative stress. Acta Med Okayama 2010; 64: 323-30.

Enomoto S, Sumi M, Kajimoto K, Nakazawa Y, Takahashi R, Takabayashi C, Asakura T, Sata M. Long-term patency of small-diameter vascular graft made from fibroin, a silk-based biodegradable material. J Vasc Surg 2010; 51: 155-64.
Yamagata T, Yoshizawa J, Ohashi S, Yanaga K, Ohki T. Expression patterns of microRNAs are altered in hypoxic human neuroblastoma cells. Pediatr Surg Int 2010; 26: 1179-84.

Reviews and Books

Lipsitz EC, Veith FJ, Ohki T. Chapter 5 Reducing radiation exposure during endovascular procedure In: Moor WS, Ahn SS, editors. Endovascular surgery 4th ed. Philadelphia: Saunders Elsevier; 2010. p. 41–7.

Kanaoka Y, Ohki T, Veith FJ. Abdominal aortic disease. In: Schillinger M, Minar E, editors. Complex cases in peripheral vascular interventions. London: Informa Healthcare; 2010. p. 131-42.

Sumi M, Ohki T. Chapter 85 Technique: Endo-

vascular therapeutic. In: Cronenwett J, Johnston W, editors. Rutherford's vascular surgery. 7th ed.

Philadelphia: Saunders Elsevier; 2010. p. 1277-94.