

Department of Surgery

Division of Pediatric Surgery and Vascular Surgery

Takao Ohki, *Professor and Chairperson*
 Yuji Kanaoka, *Assistant Professor*
 Joji Yoshizawa, *Assistant Professor*

Atsushi Ishida, *Associate Professor*
 Naoki Toya, *Assistant Professor*
 Shuichi Ashizuka, *Assistant Professor*

General Summary

Pediatric Surgery

Surgery for children at The Jikei University Hospital is offered by a highly trained, expert team of pediatric surgical professionals who specialize in the diseases and conditions affecting young people. Our surgeons work exclusively with infants, children, and adolescents and understand their unique needs.

Vascular Surgery

Research projects of our department have focused on the development of the endovascular repair of aneurysms, the 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: Children undergoing surgery often have congenital anomalies. Lectures in pediatric surgery for students are based on embryology.

Education for training physicians: Three objectives for training physicians in pediatric surgery are: 1) learning how to obtain blood samples from pediatric patients, 2) understanding fluid therapy for pediatric patients, and 3) learning how to bury sutures.

Education for surgical residents: Residents are able to act as lead surgeons or assistants during pediatric surgery.

2. Clinical study

Minimally invasive and scarless surgeries

a. Endoscopic treatment for vesicoureteral reflux using Deflux[®]

There are 3 options for managing or treating vesicoureteral reflux. We select treatment with Deflux[®] (Oceana Therapeutics, Ltd., Dublin, Ireland), an injectable dextranomer/hyaluronic acid copolymer. Treatment was successful in 2 of 3 cases.

b. Laparoscopic percutaneous extraperitoneal closure for inguinal hernia: the learning curve for attending surgeons and residents

Laparoscopic percutaneous extraperitoneal closure for pediatric inguinal hernia is a simple technique in which a purse-string suture made of nonabsorbable material is placed extraperitoneally around the hernia orifice by means of a special suture needle (Lapa-

Her-Closure™, Hakko Co., Ltd., Medical Device Division, Chikuma, Nagano, Japan). Concerns have been raised about the extensive learning curve for both attending surgeons and residents to master this technique. This study assessed the difference in learning curves for the safe performance of laparoscopic percutaneous extraperitoneal closure by attending surgeons and residents.

c. The Nuss procedure for treating pectus excavatum aims to force the sternum forward and hold it in place with an implanted steel bar without requiring 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 in our department is the third highest in Japan.

3. Basic studies

a. MicroRNAs transported by exosomes in body fluids as mediators of intercellular communication in human neuroblastoma

Cancer-cell communication is an important and complex process, achieved through a diversity of mechanisms that allows tumor cells to mold and influence their environment. Accumulating evidence indicates that cells communicate via the release and delivery of microRNAs packed into tumor-released exosomes. Understanding the role and mode of action of microRNAs from tumor-released exosomes is of paramount importance in the field of cancer biomarker discovery and for the development of new biomedical applications for cancer therapeutics.

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) in Japan. The surgical mortality rate following open surgery for the treatment of AAAs is satisfactory, but that for the treatment of 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 and branched thoracic arch stent grafts

We have developed a new minimally invasive operation for aortic arch aneurysms. After carotid-carotid bypass surgery, if needed, is performed and stent grafts are placed, a needle is used to prick the stent graft through 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. We also use branched thoracic arch stent grafts that are commercially available in Europe for endovascular repair of aortic arch aneurysms after

receiving approval from our institutional review board.

3. Research on drug-eluting stents 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. We participated in this trial. After the trial’s 1-year primary endpoint was reviewed, the Zilver PTX received approval from the Japanese Pharmaceuticals and Medical Devices Agency in January 2012 and is now available in Japan.

4. Clinical study of specific antibodies against 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 the 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.

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.

5. Research on prevention of reperfusion injury during endovascular aneurysmal repair

Large sheaths are usually used 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 inserted a small sheath into the distal side of the femoral artery, and created a shunt to supply blood flow to the distal lower extremities and to prevent complete ischemia of the lower extremities and consequent reperfusion syndrome.

Publications

Yoshizawa J, Ashizuka S, Kuwashima N, Kurobe M, Tanaka K, Ohashi S, Hiramatsu T, Baba Y, Kanamori D, Kaji S, Ohki T. Laparoscopic percutaneous extraperitoneal closure for inguinal hernia: learning curve for attending surgeons and residents. *Pediatr Surg Int.* 2013; **29**: 1281-5.

Kurobe M, Yoshida K, Asizuka S, Yoshizawa J, Ohki T. Laparoscopic Nissen fundoplication in neurologically impaired children. *Jikeikai Medical Journal.* 2013; **60**: 23-8.

Tanaka K, Nakada T, Inagaki T, Akiba T. Excision of esophageal duplication cyst in children. *Jikeikai Medical Journal.* 2013; **60**: 73-6.

Ito K, Ashizuka S, Kurobe M, Ohashi S, Kuwashima N, Yoshizawa J, Ohki T. Delayed primary reconstruction of esophageal atresia and distal tracheoesophageal fistula in a 471-g infant. *Int J Surg Case Rep.* 2013; **4**: 167-9.

Toya N, Kanaoka Y, Ohki T. Secondary interventions following endovascular repair of abdominal aortic aneurysm. *Gen Thorac Cardiovasc*

Surg. 2014; **62**: 87-94.
Toya N, Baba T, Kanaoka Y, Ohki T. Embolic complications after endovascular repair of abdominal aortic aneurysms. *Surg Today.* 2014; **44**: 1893-9. Epub 2013 Nov 26.

Sumi M, Tateishi N, Shibata H, Ohki T, Sata M. Quercetin glucosides promote ischemia-induced angiogenesis, but do not promote tumor growth. *Life Sci.* 2013; **93**: 814-9.