

## Department of Surgery

### Division of Pediatric Surgery and Vascular Surgery

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#### 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 endovascular repair of aneurysms, treatment of peripheral arterial disease with drug-eluting stents, and clinical study of specific antibodies for heparin-platelet factor 4 (PF4) complexes.

#### Research Activities

##### *Pediatric Surgery*

##### 1. Education

Education for medical students: Many children undergoing surgery have congenital anomalies. Therefore, lectures in pediatric surgery for students are based on embryology. Three students have attended overseas lectures at the Department of Pediatric Surgery of Stanford University.

Education for training doctors: Three objectives for training doctor in pediatric surgery are: 1) how to obtain a blood sample from pediatric patients, 2) understanding fluid therapy for pediatric patients, and 3) learning how to create buried sutures.

Education for surgical residents: Residents are able to perform as operators or assistants for pediatric surgery

##### 2. Clinical studies

##### a. Endoscopic treatment for vesicoureteral reflux using Deflux<sup>®</sup>

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

##### b. Electrolytes and acid-base balance in laparoscopic surgery

Carbon oxide produces changes in electrolytes and the acid-base balance in laparoscopic surgery.

##### c. In severe cases of 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 the postoperative recovery time is shorter. The number of neurologically handicapped children treated at our hospital for gastroesophageal reflux has been increasing.

d. The Nuss procedure for treating pectus excavatum aims to force the sternum forward and hold it there 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 research

#### a. Laparoscopic surgery contributes to global warming

Carbon dioxide, the most important greenhouse gas, is indispensable for laparoscopic surgery. To assess CO<sub>2</sub> emissions, we first determined the number of laparoscopic operations performed in Japan. Next, we measured the quantity of CO<sub>2</sub> used in our hospital.

#### b. Inhibitory effects of antiangiogenesis drugs on the metastasis of human neuroblastoma

The loss of antiangiogenesis factors was discovered. We evaluated the effects of several potent antiangiogenesis drugs on the metastasis of neuroblastoma in a mouse model of liver metastasis.

#### c. Plasmapheresis in severe sepsis or septic shock

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

### *Vascular Surgery*

#### 1. Development of endovascular repair of thoracoabdominal aneurysm

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

#### 2. Development of endovascular repair of aortic arch aneurysm: Retrograde in-situ branched surgery

We have developed a new minimally invasive operation for aortic arch aneurysm. After carotid-carotid bypass surgery is performed and stent graft are placed, a needle is used to push 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 fash-

ion). 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 aneurysm.

### 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 for treating 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.

We participated in a global registry and randomized controlled trial with patients from United States, Germany, and Japan which reached its 1-year primary endpoint in August 2009. With this trial, the Zilver PTX received approval from the Japanese Pharmaceuticals and Medical Devices Agency in January 2012 and will soon be 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 the 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 against 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 2012.

### 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

**Dake MD, Ansel GM, Jaff MR, Ohki T, Saxon RR, Smouse HB, Zeller T, Roubin GS, Burket MW, Khatib Y, Snyder SA, Ragheb AO, White JK, Machan LS; Zilver PTX Investigators.** Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv.* 2011; **4**: 495-504.

**Nagano Y, Fukushima T, Okemoto K, Tanaka K, Bowtell DD, Ronai Z, Reed JC, Matsuzawa S.** Siah1/SIP regulates p27(kip1) stability and cell migration under metabolic stress. *Cell Cycle.* 2011; **10**: 2592-602.

**Yoshizawa J, Negishi Y, Matsumoto Y, Ueoka R, Ohki T.** Inhibitory effect of drug-free hybrid liposomes on metastasis of human neuroblastoma. *Pediatr Surg Int.* 2011; **27**: 379-84.