

Department of Surgery

Division of Pediatric Surgery and Vascular Surgery

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General Summary

Vascular surgery

1. Development of angiogenic therapy in ischemic disease

Angiogenesis, the process of postnatal neovascularization, is a critical component of several human diseases, including ischemic heart disease, cancer, diabetic microvascular disease, and rheumatoid arthritis. Moreover, angiogenesis is believed to be mediated by the proliferation, migration, and remodeling of endothelial progenitor cells (EPCs). Recent studies have shown that EPCs increase by direct injection of EPCs and stimulation with various cytokines and that administration of drugs have lead to improvement in ischemic diseases. Here, we investigated the effects of new drugs or stem cells on angiogenesis in ischemic disease.

2. Development of new vascular grafts and stents

The patency rate of small-caliber artificial blood vessels remains low, and the use of autologous venous grafts is inevitable, yet large venous autografts, such as the great saphenous vein, are often not available. Therefore, we are performing a study to develop new vascular grafts with intraluminally grown autologous vascular endothelial cells and with biodegradable materials. Moreover, we will develop biodegradable stents and drug-eluting stents.

3. Research on hemostatic fleece and closure devices in endovascular aortic aneurysm repair

We have found that collagen patches coated with components of fibrin glue significantly reduce blood loss and the time required for hemostasis at the operation site in endovascular aortic aneurysm repair. Moreover, percutaneous aortic aneurysm repair has been shown to be technically feasible and to be associated with a low morbidity rate. Complications from percutaneous arterial closure are not insignificant, however, and can be life-threatening. We have evaluated our experiences with this technique, compared them with previously published results, and identified factors associated with complications and conversion to open repair.

4. Clinical study of specific antibody for heparin-platelet factor 4 complexes

Heparin is commonly used for anticoagulation in vascular surgery. Heparin-induced thrombocytopenia 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-platelet factor 4 (PF4) complexes. Patients with such antibodies are at increased risk for heparin-induced thrombocytopenia. 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, particularly in patients undergoing major vascular surgery. The results of this study will be published in late 2007.

Pediatric surgery

The Jikei University Hospital is authorized (has been certified?) by the Japanese Society of Pediatric Surgeons. Operations for children at The Jikei University Hospital are performed by a highly trained, expert team of surgical professionals who specialize in the diseases and conditions affecting young people. Four specialists in pediatric surgery work at our hospital. In 2006, 346 patients were admitted, and 272 patients underwent surgery. The numbers of patients are increasing yearly.

Our pediatric surgery team for minimally invasive surgery is a leader in developing and performing minimally invasive procedures on children in Japan. To perform minimally invasive surgery, our team uses specially designed instruments that are inserted through small, bandage-sized incision, especially for gastroesophageal reflux, inguinal hernias, funnel chest, and vesicourethral reflux. Minimally invasive procedures are as effective as open operations, take no more time, and cost no more. They typically require shorter hospitalization after surgery, reduce postoperative pain, shorten recovery time, and leave smaller, less noticeable scars.

Research Activities

Vascular surgery

1. Therapeutic angiogenesis has emerged as a promising therapy to treat patients with ischemic diseases. Transplantation of bone marrow cells is reported to augment development of collateral circulation in ischemic organs either by differentiating into vascular cells or by secreting angiogenic cytokines. Recent evidence suggests that adipose tissues secrete several humoral factors and contain pluripotent stem cells. We evaluated the therapeutic potential of cells derived from adipose tissue to promote angiogenesis in cases of ischemia.
2. Plasma levels of high-density lipoprotein (HDL) are negatively correlated with the incidence of ischemic diseases. However, the molecular mechanism by which HDL prevents atherosclerosis is not fully understood. We investigated the effect of HDL on differentiation of EPCs and angiogenesis in ischemia.
3. There is an increasing need for functional small-diameter grafts for surgical revascularization. However, smaller vascular grafts made from synthetic biomaterials, particularly smaller than 6 mm in diameter, are associated with a high incidence of thrombosis. Fibroin is a biodegradable protein derived from silk which provides an antithrombotic surface and serves as a scaffold for various cell types in tissue engineering. We evaluated the potential of fibroin to generate artificial vascular prostheses for small arteries.

Pediatric surgery

To improve treatment results, new approaches are essential. One new approach is the use of gene therapy, and another new method is the inhibition of tumor angiogenesis. This year, we focused on gene therapy with tumor immunology using dendritic cells that induced mouse interferon (IFN)-alpha/beta with an adenovirus vector (Adm IFN-Alfa) in mice bearing GL26 sarcoma. Tumor-specific cytotoxic T lymphocytes were induced after injection of Adm IFN-alpha into GL26 sarcoma. Also when we used mice bearing MCA205 sarcoma, tumor size was decreased after injection of Adm IFN-alpha.

We presented these results at the annual meetings of the Japan Surgical Society, the Japanese Cancer Association, and the Japanese Society of Pediatric Surgeons. Our article entitled "Inhibitory effect of drug-free hybrid liposomes on metastasis of human neuroblastoma" won the annual best-article prize of the Japanese Society of Pediatric Surgeons.

Publications

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