

Department of Surgery

Division of Digestive Surgery

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General Summary

The delivery of research papers is supported by writing skills in addition to the ability to accomplish the study. More efforts to read scientific papers are necessary to improve writing skills and to ensure patient safety. All surgeons should keep in mind that research based on anatomic, pathologic, and physiologic principles, in combination with animal experimentation, makes it possible to develop complex operative procedures and to become the consummate surgeon, as stated in the last Southern Surgical Association Presidential Address (J Am Coll Surg 2015; 220(4); 387-395).

Research Activities

Upper gastrointestinal surgery

We have started to investigate the effect of preoperative chemotherapy with fluorouracil, cisplatin, and docetaxel for advanced esophageal cancer. We still focus on reducing complications after esophagectomy; specifically used are an intraoperative thermal imaging system to evaluate the gastric tube and a recurrent nerve integrity monitoring to confirm vocal cord movement. In addition, we are planning to investigate the change of body composition in relation to esophagectomy.

Esophageal manometry and 24-hour pH study were used to evaluate pathophysiology of benign esophageal disorders. We have proposed “laparoscopic circumferential Heller myotomy” as a novel approach to relieve chest pain in patients with achalasia and are conducting a prospective research study to expand evidence of this new surgical technique.

We are continuing to evaluate the usefulness of sentinel lymph node navigation and reduction surgery for early gastric cancer. We are aiming for radical cure and functional preservation by using a sentinel lymph node search method with a fluorescent infrared endoscope and radioisotope. In order to elucidate the mechanism of lymph node metastasis(LNM) in gastric cancer, immunohistochemical staining of lymphatic vessels is performed using past surgical specimens to examine the lymphatic vessel infiltration form of cancer cells, and risk factors of LNM were reexamined. The risk factors for postgastric resection syndrome and examination according to the surgical method are also important issues, and patients who have undergone gastrectomy more than 1 year ago are evaluated with the C13 breath test. We are investigating risk factors for metastasis by performing various types of immunostaining and the real-time reverse-transcriptase polymerase chain reaction focusing on the expression of various vascular endothelial growth factors. Treatment for obesity is performed by a team (dietician, pharmacist, and physicians), and patients with resistant to weight loss despite nutritional guidance undergo surgery. The change of gastroesophageal reflux before and after sleeve gastrectomy is assessed with 24 hours pH monitoring.

Lower gastrointestinal surgery

In collaboration with the Department of Internal Medicine we hold regular conferences and examine multimodal therapy for colorectal cancer. We have been investigating operative methods, complications, and histopathological factors with a database of patients with colorectal cancer. We started studies of anal function by means of stationary 3-dimensional manometry and aim at specific treatment for anal disease and postoperative complications. We are developing a complementary DNA library from surgical specimens and preparing a database for basic researches.

In collaboration with the Department of Biochemistry, we analyzed the expression of intracellular signal molecules that are associated with the progression and growth of cancer. We analyzed the involvement of dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 2 (DYRK2) in the induction of apoptosis and the control of the cell cycle. By correlating with the database, we investigated the relationship of DYRK2 expression and associated genes. We prepared 3-dimensional cultures with colorectal cancer specimens to form so-called organoids, with which we started basic research on the mechanism of drug action. Our aim is to develop methods to choose the appropriate medicine before treatment.

Tumors are believed to have cancer stem cells, which have self-replication ability and multipotency and to cause recurrence, metastasis, and resistance to anticancer drugs and radiotherapy. We pay attention to provirus integration site for Moloney murine leukemia virus 1 (Pim-1), which is identified from mouse T-cell lymphoma, and analyzed its function in colorectal cancer, particularly the mechanism about the characteristics acquisition of stem cells.

Hepatobiliary and pancreatic surgery

The outlines of our main research activities are as follows:

1. Living donor liver transplantation (LDLT) and regenerative medicine

2. Treatment for hepatocellular carcinoma (HCC) and controlling recurrence
3. Chemotherapy for pancreatic and biliary cancers
4. Expansion of surgical indications for multiple hepatic tumors
5. Laparoscopic surgery for the liver, biliary tree, pancreas, and spleen
6. Navigation surgery for hepatobiliary and pancreatic diseases
7. Nutritional therapy for patients with cancer (enhanced recovery after surgery)
8. Control of surgical site infection
9. Effect of preoperative treatment of eltrombopag on splenectomy for idiopathic thrombocytopenic purpura
10. Molecular-targeting therapy for advanced HCC
11. Analyses of new biological tumor markers for HCC

Since 2007 we have performed LDLT for 24 patients, including 4 patients who underwent ABO-incompatible LDLT. All 24 recipients were discharged in good condition on postoperative days 15 to 146, and donors were discharged on postoperative days 7 to 32 and returned to preoperative status. We are planning to extend the indications of LDLT to acute hepatic failure. The outcome of patients who undergo HCC resection at our institution is much better than the national average. To reduce postoperative complications, we investigate the risk factors and effective treatments for postoperative portal vein thrombosis and venous thromboembolism. We have performed clinical trials for pancreatic cancer (combination chemotherapy with gemcitabine, S-1 with regional arterial infusion of nafamostat mesilate for advanced pancreatic cancer, and gemcitabine in combination with regional arterial infusion of nafamostat mesilate as an adjuvant chemotherapy after pancreatectomy) and biliary tract cancer (chemotherapy with S-1 every other day in combination with gemcitabine/cisplatin). We have also performed extended liver resections as a conversion therapy for multiple metastatic tumors of the liver, mainly originating from colorectal cancers. Furthermore, laparoscopic surgery, including hand-assisted laparoscopic surgery and laparoscopy-assisted, i.e., hybrid surgery, has gradually been expanded for hepatobiliary, pancreatic, and splenic diseases because of its lower invasiveness. We have used the SYNAPSE VINCENT medical imaging system for 3-dimensional visualization and preoperative planning for operative safety. Furthermore, hepatobiliary and pancreatic navigation surgery using augmented reality for either open or laparoscopic surgery is performed at Daisan Hospital with the Institute for High Dimensional Medical Imaging Research Center. With regard to nutritional therapy for patients who have cancer, clinical and experimental studies are examining enhanced recovery after surgery, surgical site infection, and the use of eltrombopag before laparoscopic splenectomy for idiopathic thrombocytopenic purpura.

Digestive surgery (comprehensive)

We have been pursuing clinical research at 4 university hospitals. Since 2014, we have had 6 articles published in English.

Because surgical infection is common problem that is important to control, we have assigned members of the staff to be in charge of surgical infection at each university hospital and are encouraging the reduction of surgical infection. Three of the 4 hospitals are participating in the Japan Nosocomial Infections Surveillance program supervised by the

Japanese Ministry of Health, Labour and Welfare, and 3 of the 4 hospitals are teaching hospitals approved by the Japan Society for Surgical Infection. Although we are active in presentations at national conferences, we must publish articles other than case reports.

Publications

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