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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 evaluate the pathogenesis of primary esophageal motor functional disorders, especially achalasia and gastroesophageal reflux disease, using high-resolution manometry and multichannel intraluminal impedance pH monitoring. We have performed many laparoscopic operations and obtained good results. Recently, we introduced reduced port surgery and needlescopic surgery for minimally invasive surgery. Furthermore, we have started Per-Oral Endoscopic Myotomy (POEM) for achalasia since 2016. Taking into account the needs and pathophysiology, the best treatment for patients is selectively performed. Basic research in esophageal cancer led us to find molecular markers that indicate patients' prognoses. We aimed to investigate the significance of small ubiquitin-like modifier 1 (SUMO-1) expression in esophageal cancer as a prognostic factor. We found that

overexpression of SUMO-1 correlated with malignancy-associated pathological findings and poor prognoses. We continue to assess viability of the gastric tube using intraoperative thermal imaging system during esophagectomy. Correlation between suitable graft construction and postoperative complications of a graft was then investigated. We also continue to examine intraoperative recurrent nerve monitoring in order to prevent postoperative recurrent nerve palsies as well as to predict degree of paralysis after surgery. We started to analyze upper esophageal sphincter and residual esophageal motility since 2016 by high resolution manometry. We started providing minimum invasive surgery for patients with early gastric cancer through sentinel node navigation surgery (SNNS) in 2001. We have conducted more than 300 cases of such operations until now. We developed SNNS using infrared ray endoscopic system for the first time in the world. In addition, we have conducted surveying biological cancer behavior using immunohistochemical and RT-PCR methods, which revealed that zinc finger protein (ZNF) 217 was an independent prognostic factor for relapse-free survival and a novel prognostic biomarker for patients with gastric cancer. Postgastrectomy syndrome comprises specific symptoms after gastrectomy and is a target for treatment. To decrease the incidence and severity of postgastrectomy syndrome and to maximize residual gastric function, several types of limited gastric resection with refined techniques of reconstruction have been attempted. In addition, after gastrectomy, multiple tests of postoperative gastrointestinal function are performed to evaluate various types gastrectomy procedures. We also started sleeve gastrectomy for morbid obesity.

Lower gastrointestinal surgery

We have reported the beneficial cosmetic outcomes of a novel and patient-friendly ileostomy procedure. This procedure uses the umbilical fossa for placement of a defunctioning ileostomy followed by a simple umbilicoplasty for ileostomy closure. In collaboration with the Department of Internal Medicine we hold conference and register the database of chemotherapy to examine combined therapy for the colorectal cancer. We started studies on anal function using Stationary 3D-manometry. Together with the Department of Biochemistry we are committed to construct a complementary DNA library from the surgical specimens of colorectal cancer to analyze the expression of intracellular signal molecules that are associated with progression and growth of cancer. As a first step of the project, the following basic research will be started: analysis of the cell-cycle regulation and dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 2(DYRK2) in relation to c-jun/c-myc phosphorylation. By correlating with the clinical database the relationship between the stage of colorectal cancer and the manifestation of DYRK2 and associated genes is investigated. When chemoradiation therapy is performed for rectal cancer, radiation causes microenvironmental inflammation around cancer cells and promotes the secretion of matrix metalloproteinase (MMP) and nuclear factor kappa B (NF- κ B). In addition, NF- κ B is reported to directly induce MMP. The basement membrane is dissolved by MMP, and cancer cells enter the bloodstream and metastasize to other organs. Therefore, suppression of MMP might prevent metastasis after surgery. We will examine whether down regulation of NF- κ B decreases the recurrence and metastasis of colon cancer.

Hepatobiliary and pancreatic surgery

The first LDLT was successfully performed for a patient with postnecrotic cirrhosis and HCC in February 2007. Our first blood type ABO-incompatible LDLT (15th LDLT) was performed for a patient with primary biliary cirrhosis in June 2015. Our 20th LDLT was performed for a patient with primary biliary cirrhosis in March 2017. All 20 recipients were discharged in good condition on postoperative day 15 to 70, and donors were discharged on postoperative day 7 to 26 and returned to preoperative status. We are planning to extend the indication of LDLT to acute hepatic failure. The 5-year cumulative overall survival rate of HCC after hepatic resection in our department is 75%, which is significantly better than the mean survival rate in Japan (56.8%). We have performed clinical trials for pancreatic cancer and biliary tract cancer. Ongoing trials for pancreatic cancer are evaluating 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. A current trial for advanced biliary tract cancer is evaluating 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. Navigation for liver resection has been paid for by national health insurance since April 1, 2012, and the Vincent navigation system was introduced in July 2012. Biliary and pancreatic navigation surgery for either open or laparoscopic surgery is performed 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.

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