

Department of Surgery

Division of Digestive Surgery

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General Summary

We researchers in the academic environment must be familiar with statistical tests, including linear and logistic regression analyses.

Although a large number of basic and clinical studies were published by our division from April 2013 through March 2014, we must make greater efforts to publish articles in journals with high impact factors. Thomas Wakley, the founder of *The Lancet*, said, “A lancet can be an arched window to let in the light or it can be a sharp surgical instrument to cut out the dross and I intend to use it in both senses.”

Research Activities

Upper gastrointestinal surgery

We are attempting to evaluate the pathogenesis of primary esophageal motor functional disorders, such as achalasia and gastroesophageal reflux disease, using high-resolution manometry and multichannel intraluminal impedance pH monitoring. We have started to use mesh to reinforce the hiatus in esophageal hiatal hernia repair. Because a correlation is strongly suspected between the viability of the gastric tube assessed with an intraoperative thermal imaging system during esophagectomy for esophageal cancer and the postoperative complication rate of a graft, such imaging has become standard practice. To reduce the rates of postoperative recurrent nerve palsy, we continue to monitor the activity of the recurrent nerve during surgery; the results will be analyzed and will be published soon.

To ensure the benefits of laparoscopic sentinel-node navigation surgery with an infrared endoscope for early gastric cancer, we are collecting data to compare the outcomes of conventional surgery and less invasive surgery. We have started to perform various types of immunohistochemical staining and to examine the expression of messenger RNA in tumor cells. We found that zinc finger protein 217 was an independent prognostic factor for relapse-free survival in patients with gastric cancer, which might be used as a

novel prognostic biomarker of 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, multiple postoperative gastrointestinal function tests are applied to patients who have undergone gastrectomy to evaluate various gastrectomy procedures and to inform the patients of the appropriate management.

Lower gastrointestinal surgery

We assessed surgeons' stress during laparoscopic surgery for colorectal cancer by measuring blood levels of adrenaline, noradrenaline, dopamine, ACTH, and cortisol. We are analyzing the data to determine which factors are related to surgeons' stress during an operation. We have published an article describing the excellent cosmetic outcome of a novel patient-friendly ileostomy procedure. This procedure uses the umbilical fossa for placement of a defunctioning ileostomy followed by a simple umbilicoplasty for ileostomy closure. A collaborative study with the Department of Urology to identify novel cancer-related proteins of the gastrointestinal tract is ongoing. The relationship between copy number variation and the recurrence/prognosis is evaluated after the extraction of DNA from frozen specimens of colorectal cancer tissue, because copy number variation may influence gene functions. In collaboration with the Department of Biochemistry, we are constructing 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 colorectal cancer. As a first step of this project, the following basic research will be started: analyses of cell-cycle regulation and dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase (DYRK) in relation to c-jun/c-myc phosphorylation. In addition to these analyses, we will strengthen the foundation of our future basic research by applying the complementary DNA library and by constructing clinical database.

Hepatobiliary and pancreatic surgery

The outlines of our main research activities are as follows:

1. Live donor liver transplantation (LDLT) and regenerative medicine
2. Treatment for hepatocellular carcinoma and control of recurrence
3. Chemotherapy for pancreatic and biliary cancer
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 with eltrombopag after splenectomy for idiopathic thrombocytopenic purpura
10. Molecularly targeted therapy for advanced hepatocellular carcinoma
11. Analyses of new biological tumor markers for hepatocellular carcinoma

The first LDLT was successfully performed for a patient with postnecrotic cirrhosis and hepatocellular carcinoma on February 9, 2007. Our 13th LDLT was performed for a patient with primary biliary cirrhosis on May 31, 2013. All 13 recipients were discharged in good condition on postoperative days 15 to 55, and all donors were discharged on postoperative day 8 to 26 and returned to their preoperative status. We are planning to extend the indications of LDLT to blood type-ABO incompatible transplants and to acute hepatic failure. In our department, the 5-year cumulative overall survival rate after hepatic resection for hepatocellular carcinoma is 70%, which is significantly better than the nationwide data of 52% in Japan.

We have performed translational research on combination chemotherapy with gemcitabine and a new protease inhibitor, nafamostat mesylate, which is associated with both the inhibition of nuclear factor κ -B and the induction of apoptosis in pancreatic cancer cell lines. We have started a new combination chemotherapy protocol with gemcitabine, TS-1, and nafamostat mesylate for advanced pancreatic cancer.

We have also performed extended liver resections as conversion therapy to multiple metastatic liver tumors, mainly originating from colorectal cancers. Otherwise, the indications for laparoscopic surgery, including hand-assisted laparoscopic surgery and laparoscopy-assisted, i.e., hybrid surgery, to hepatobiliary, pancreatic, and splenic diseases have been gradually expanded due to its lesser invasiveness. Navigation for liver resection has been covered by national health insurance since April 1, 2012, and the Vincent navigation system was introduced in July 2012. Biliary and pancreatic navigation surgery is performed with the Institute for High Dimensional Medical Imaging Research Center. Clinical as well as experimental studies including nutritional therapy for patients with cancer, enhanced recovery after surgery, surgical site infection, and the use of eltrombopag before laparoscopic splenectomy for idiopathic thrombocytopenic purpura are ongoing. Also, we have started to apply molecularly targeted therapy to advanced hepatocellular carcinoma and to analyze new biological markers for hepatocellular carcinoma.

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