

## Department of Surgery

### Division of Digestive Surgery

---

Katsuhiko Yanaga, *Professor*  
 Kazuhiko Yoshida, *Professor*  
 Nobuyoshi Hanyu, *Associate Professor*  
 Norio Mitsumori, *Associate Professor*  
 Kazuo Matai, *Associate Professor*  
 Yoshiyuki Furukawa, *Assistant Professor*  
 Kouji Nakada, *Assistant Professor*  
 Yuichi Ishida, *Assistant Professor*  
 Takeyuki Misawa, *Assistant Professor*  
 Yoshiaki Kita, *Assistant Professor*  
 Hidejirou Kawahara, *Assistant Professor*  
 Naoto Takahashi, *Assistant Professor*

Hideyuki Kashiwagi, *Professor*  
 Susumu Kobayashi, *Professor*  
 Tetsuji Fujita, *Associate Professor*  
 Tomoyoshi Okamoto, *Associate Professor*  
 Akira Yanagisawa, *Assistant Professor*  
 Yuji Ishii, *Assistant Professor*  
 Shuzo Kono, *Assistant Professor*  
 Yoichi Toyama, *Assistant Professor*  
 Yoshio Ishibashi, *Assistant Professor*  
 Noburo Omura, *Assistant Professor*  
 Yoshiyuki Hoya, *Assistant Professor*

### General Summary

Last year, an interesting paper appeared in *The Lancet* which reported that 234 million major surgical procedures are performed worldwide each year, or 1 for every 25 people. This figure is more than twice that of yearly births and 7 times the 33.2 million people infected with human immunodeficiency virus. The increasing number of operations is associated with the introduction of new surgical techniques and refinements in perioperative care, such as laparoscopic cholecystectomy and a less-liberal fluid regimen for fast-track colonic surgery. These advances could be achieved by performing high-quality studies, including randomized controlled trials. Important scientific findings derived from experimental and clinical research should be published in academic journals.

To assess trends in our surgical research activity, we performed an advanced Web search with Medline using several key words, such as “Jikei,” “surgery,” and “English language.” The search yielded 59 peer-reviewed articles from April 1, 2008, to March 31, 2009, a higher number than in any previous year. For example, the number of articles published from April 1, 2004 to March 31, 2005, was only 22. However, when the search is limited to core clinical journals, such as *Annals of Surgery* and *Archives of Surgery*, only 24 articles are found over a 10-year period. Consequently, we should continue to try to increase the quality of our research.

### Research Activities

#### *Upper gastrointestinal surgery*

The advantages and disadvantages of each method of laparoscopic surgery for achalasia and reflux esophagitis were carefully assessed, because the reputation for our technique has enabled us to evaluate many patients in spite of the rare nature of these diseases. Basic research in esophageal cancer has led us to discover molecular markers indicating prognosis.

We have established a new technique of sentinel node navigation surgery without radioisotopes for early gastric cancer using indocyanine green under infrared ray observation. A multicenter trial to evaluate our technique with infrared ray laparoscopy systems has been performed. The sentinel node detection rate, accuracy, and sensitivity were 100%. This method is safe and efficient.

### *Colorectal surgery*

To improve the quality of laparoscopic operations we are evaluating the usefulness and reliability of the Virtual Reality Surgical Simulator for laparoscopic colectomy. We are also examining the relationship between the reactions of various immunoglobulins in the serum of patients with cancer by means of enzyme-linked immunosorbent assay and several factors relevant to cancer status. We are using the [ $^{13}\text{C}$ ]-breath test to evaluate bowel function after colorectal surgery and to determine the appropriate duration of postoperative bowel rest. Preoperative diagnosis of lymph-node metastasis for colorectal cancer with diffusion magnetic resonance imaging (D-MRI) is ongoing. A total of 119 patients (52 with rectal cancer and 67 with colon cancer) were enrolled. Lymph-node metastases were judged with D-MRI and were compared with the pathological results. The form of metastasis was classified as abundant or scarce. We had discussed the results at the end of 1 year (period I,  $n=79$ ) and re-audited the sensitivity and specificity after our meeting (period II,  $n=40$ ). It was related with the ability of D-MRI to detect metastasis (period I: sensitivity=61%, specificity=73%, positive predictive value [PPV]=55%, and negative predictive value [NPV]=77%; period II: sensitivity=79%, specificity=95%, PPV=94%, and NPV=83%). The specificity and PPV for period II were significantly higher than those for period I ( $p<0.05$ ). In period I and period II, respectively, the mean diameters of lymph nodes that D-MRI indicated were metastatic (i.e., "positive") were  $10.3\pm 5.4$  mm (range, 3–28 mm; 32 nodes) and  $9.1\pm 3.0$  mm (range, 4–14 mm; 16 nodes); those of true-positive nodes were  $11.5\pm 6.2$  mm (range, 4–28 mm; 18 nodes) and  $9.2\pm 3.1$  mm (range, 4–14 mm; 15 nodes); and those of false-positive nodes were  $6\pm 3.8$  mm (range, 3–14 mm; 14 nodes) and 8 mm (1 node). On the other hand, the diameters of lymph nodes that D-MRI indicated were nonmetastatic (i.e., "negative") in period I and period II, respectively, were  $5.9\pm 2.4$  mm (range, 3–16 mm; 47 nodes) and  $5.7\pm 2.8$  mm (range, 2–15 mm; 24 nodes); those of true-negative nodes were  $5.9\pm 2.1$  mm (range, 3–16 mm; 36 nodes) and  $5.3\pm 2.1$  mm (range, 2–8 mm; 20 nodes); and those of false-negative nodes were  $5.7\pm 2.7$  mm (range, 3–12 mm; 11 nodes) and  $7.8\pm 4.9$  mm (range, 4–15 mm; 4 nodes). We have concluded that hot nodules with a diameter 9 mm or greater are clearly metastatic.

### *Hepatobiliary and pancreatic surgery*

The outlines of our main research activities in the field of hepatobiliary and pancreatic surgery are as follows: 1) living donor liver transplantation (LDLT), regenerative medicine, and artificial liver (especially, implantable artificial liver); 2) chemotherapy for advanced pancreatic cancer; 3) expansion of surgical indications for multiple hepatic tumors by hepatic resection; and 4) laparoscopic resection of the liver, pancreas, and spleen.

The first LDLT was successfully performed for a patient with cirrhosis and postnecrotic hepatocellular carcinoma on February 9, 2007. Our sixth LDLT was performed for a patient with primary biliary cirrhosis on January 16, 2009. All six recipients were discharged 19 to 32 days after surgery and had a good clinical course. Our ongoing research on regenerative medicine and artificial organs is expected to have a synergistic effect on liver transplantation medicine. We have performed translational research through combination chemotherapy with gemcitabine and the naive protease inhibitor FUT-175, which has the dual functions of nuclear factor  $\kappa$ B inhibition and apoptosis induction in pancreatic cancer cell lines. Regarding other issues described above, clinical and experimental studies are ongoing after being approved by the Ethics Committee of The Jikei University.

## Publications

- Shinohara T, Kashiwagi H, Yanagisawa S, Yanaga K.** A simple and novel technique for the placement of anti-adhesive membrane in laparoscopic surgery. *Surg Laparosc Endosc Percutan Tech* 2008; **18**: 188-91.
- Shinohara T, Fujita T, Misawa T, Sakamoto T, Yoshida K, Kashiwagi H, Yanaga K.** Impact on laboratory training in subsequent performance of laparoscopic cholecystectomy. *Langenbecks Arch Surg* 2009; **394**: 557-62.
- Nishikawa K, Hanyuu N, Yuda M, Tanaka Y, Matsumoto A, Yasue H, Hayashi T, Kawano S, Usuba T, Iino T, Mizuno R, Iwabuchi S.** How can we control intraoperative bacterial contamination and surgical-site infection during an anterior resection or Hartmann's/Miles' operation. *J Gastrointest Surg* 2008; **12**: 1995-2000.
- Fujita T, Ishida Y, Yanaga K.** Impact of appropriateness of initial antibiotic therapy on outcome of postoperative pneumonia. *Langenbecks Arch Surg* 2008; **393**: 487-91.
- Fujita T, Namiki N.** Replacement of peripheral intravenous catheters. *J Clin Nurs* 2008; **17**: 2509-10.
- Tsuboi K, Omura N, Yano F, Kashiwagi H, Yanaga K.** Relationship of the frequency scale for symptoms of gastroesophageal reflux disease with endoscopic findings of cardiac sphincter morphology. *J Gastroenterol* 2008; **43**: 798-802.
- Kobayashi K, Shida A, Yamada H, Ishibashi Y, Nakayama R, Toriumi Y, Mitsumori N, Kashiwagi H, Yanaga K.** Frequent splicing aberration of the base excision repair gene hMYH in human gastric cancer. *Anticancer Res* 2008; **28**: 215-22.
- Yano F, Omura N, Tsuboi K, Kashiwagi H, Yanaga K.** Thoracic aortic injury during laparoscopic fundoplication for reflux esophagitis. *Int J Surg* 2008; **6**: 490-2.
- Hoya Y, Takahashi T, Saitoh R, Anan T, Sasaki T, Inagaki T, Yamazaki S, Yamashita M, Yanaga K.** Blood transfusion requirement for gastric cancer surgery: reasonable preparation for transfusion in the comprehensive health insurance system. *Int J Surg* 2008; **6**: 234-7.
- Hoya Y, Okamoto T, Fujita T, Yanaga K.** A novel drain fixation device to reduce the peritoneal drain-related complications after gastroenterological surgery. *ANZ J Surg* 2008; **78**: 1141-2.
- Okamoto T, Gocho T, Futagawa Y, Fujioka S, Yanaga K, Ikeda K, Kakutani H, Tajiri H.** Usefulness of pancreatic duct stenting prior to surgery as a guide to decide the feasibility of limited pancreatic resection. *Dig Surg* 2008; **25**: 175-8.
- Okamoto T, Gocho T, Futagawa Y, Fujioka S, Yanaga K, Ikeda K, Kakutani H, Tajiri H.** Does preoperative pancreatic duct stenting prevent pancreatic fistula after surgery?: a cohort study. *Int J Surg* 2008; **6**: 210-3.
- Ishii Y, Saito R, Marushima H, Ito R, Sakamoto T, Yanaga K.** Hepatic reconstruction from fetal porcine liver cells using a radial flow bioreactor. *World J Gastroenterol* 2008; **14**: 2740-7.
- Iida T, Shiba H, Misawa T, Ohashi T, Eto Y, Yanaga K.** Adenovirus mediated CD40L gene therapy induced both humoral and cellular immunity against rat model of HCC. *Cancer Sci* 2008; **99**: 2097-103.
- Sakurai M, Misawa T, Shiba H, Iida T, Ohashi T, Yanaga K.** A novel approach for gene transduction with adenovirus vector and the fibrin glue system. *Anticancer Res* 2008; **28**: 3809-13.
- Uwagawa T, Misawa T, Sakamoto T, Ito R, Gocho T, Shiba H, Wakiyama S, Hirohara S, Sadaoka S, Yanaga K.** A phase I study of full-dose gemcitabine and regional arterial infusion of nafamostat mesilate for advanced pancreatic cancer. *Ann Oncol* 2009; **20**: 239-43.
- Shiba H, Ishii Y, Ishida Y, Wakiyama S, Sakamoto T, Ito R, Gocho T, Uwagawa T, Hirohara S, Kita Y, Misawa T, Yanaga K.** Assessment of blood-products use as predictor of pulmonary complications and surgical-site infection after hepatectomy for hepatocellular carcinoma. *J Hepatobiliary Pancreat Surg* 2009; **16**: 69-74.

**Hanyu K, Iida T, Shiba H, Ohashi T, Eto Y, Yanaga K.** Immunogene therapy by adenovirus vector expressing CD40 ligand for metastatic liver cancer in rats. *Anticancer Res* 2008; **28**: 2785-90.

**Kawahara H, Kobayashi T, Watanabe K, Kobayashi S, Kashiwagi H, Yanaga K.** Intraoperative drainage of intestinal contents in emergency surgical treatment of left-sided colonic obstruction. *Hepatogastroenterology* 2008; **55**: 940-2.

**Ogawa M, Watanabe M, Eto K, Kosuge M, Yamagata T, Kobayashi T, Yamazaki K, Anazawa S, Yanaga K.** Poorly differentiated adenocar-

cinoma of the colon and rectum: clinical characteristics. *Hepatogastroenterology* 2008; **55**: 907-11.

#### Reviews and Books

**Kashiwagi H.** Invited commentary for "Transthoracic Collis-Nissen repair for massive type IV paraesophageal hernia". *Gen Thorac Cardiovasc Surg* 2008; **56**: 451-2.

**Fujita T.** Influence of preoperative inflammation on outcomes of colorectal cancer surgery. *Ann Surg* 2008; **247**: 1084-5.