

[43]. Surgeons performing LLR were typically in their 40s. In North America and Europe, LLR was mostly performed at academic medical centers and has undergone global diffusion after the 1st ICCLLR in 2008 [12]. Meanwhile, in Japan, the majority of surgeons performing LLR belonged to middle-tier regional hospitals, where LLR has been increasingly used since its implementation in 2009 or later, comprising up to 40% of all liver resections. The Japanese social insurance system approved LLR including partial hepatectomy and left lateral sectionectomy in April 2010. In the current study, we collected data from 1,331 patients between 2005 and 2010 from 32 institutions representative of the “Endoscopic Liver Surgery Study Group.” Surgeons participating were experienced in both liver surgery and laparoscopic surgery. In Japan, modern chemotherapy consists of oxaliplatin or irinotecan was introduced in 2005 [9]. It has been reported that administrative databases are not designed to resolve a specific scientific question and important true confounders may not be systematically recorded [36]. Therefore, we recently developed a unified database for CRLM produced by the Japanese Society of Hepato-Biliary Pancreatic Surgery and the Japanese Society of Cancer of the Colon and Rectum. We have access not only to the contents of operative data and accurate outcomes but also to information on perioperative non-surgical therapy, including chemotherapy, radiotherapy, or ablation therapy. This database can be applied also to those situations where the patients wish to change hospitals or change the treatment concept according to a personal anonymized number. We believe that this study reveals precise results on the emerging use of LLR for CRLM in Japan.

Laparoscopic liver resection may theoretically be superior to OLR in terms of good visibility of the operative field because of the magnifying effect and reduced blood loss from the hepatic vein due to pneumoperitoneum pressure [44]. On the other hand, some weak points remain, including the lack of sensation, limitation of the two-dimensional field of view and the difficulty to use long forceps or intraoperative ultrasonography. For several reasons (ethical, learning curve, lack of standardized techniques, benefits of laparoscopy across the

field of surgery, etc.), its oncological value has not yet been determined by RCT [37]. Another major hurdle to designing a RCT is that patients may not be willing to be randomized into the OLR group [31]. As far as we know, two RCTs are in progress comparing LLR and OLR; the ORANGE II PLUS trial (<http://clinicaltrials.gov/ct2/show/record/NCT01441856>) and the OSLO CoMet study (<http://clinicaltrials.gov/ct2/show/NCT01516710>) [14]. The latter is the RCT comparing LLR and OLR for CRLM, but data are not available yet.

To date, numerous retrospective, comparative studies and meta-analyses of non-RCTs have been published [15–30]. These papers tend to demonstrate longer operative time, lower estimated blood loss, and a shorter hospital stay in LLR patients compared with OLR patients. In comparison with synchronous hepatectomy and colectomy, the laparoscopic approach was associated with shorter hospitalization durations than the open approach [29]. Overall morbidity and mortality were comparable. The LLR did not affect RFS and OS for CRLM; however, one study showed better OS for LLR patients [30]. However, comparison of surgical outcomes between LLR and OLR using all patients enrolled could be considered quite unfair, because there is serious selection bias in preoperative background factors. In the current study, after PSM matching, almost all collaborates were turned to within the range of standardized difference almost 10% differences. Recently, it was reported that there is no statistically significant difference in treatment effect between non-randomized studies with appropriate PSM analysis and RCT [37]. The PSM design might be considered the best level of evidence available, especially if based on a prospectively maintained database and carried out with an intention-to-treat analysis [32].

To date, three documents have been published using PSM, confirming short-term advantages and comparable survival outcomes in LLR patients compared with OLR patients for CRLM [31–33] (Table 3). Common short-term advantages by LLR included reduced blood loss and a shorter hospital stay. One study demonstrated lower morbidity [31] and another study showed longer operating time in LLR [33]. However, in these studies, the number of CRLM patients

Table 3 Outcomes in colorectal liver metastases (CRLM) patients who underwent laparoscopic liver resection (LLR) and open liver resection (OLR) in the papers using propensity score matching

Reference number	Patients' number LLR/OLR	Operation time	Blood loss	Morbidity	Mortality	Hospital stay	RFS/DFS	OS/DSS
[31]	35 / 140	Equal	LLR lesser	LLR lesser	Equal	LLR shorter	Equal (DFS)	Equal (OS)
[32]	52 / 52	Equal	LLR lesser	Equal	Equal	LLR shorter	Equal (DFS)	Equal (OS)
[33]	36 / 36	LLR longer	LLR lesser	Equal	Equal	LLR shorter	Equal (DFS)	Equal (OS)
This paper	171 / 342	Equal	LLR lesser	Equal	Equal	LLR shorter	Equal (RFS)	Equal (OS) (DSS)

DFS disease-free survival, DSS disease-specific survival, LLR laparoscopic liver resection, OLR open liver resection, OS overall survival, RFS recurrence-free survival

undergoing LLR was small (35 to 52 patients), and several heterogeneous background factors existed. In the current study, the number of PSM-patients with CRLM undergoing LLR was 171, and the majority of background factors were matched. PSM matching was performed for the patients in the same period (2005 to 2011), and the survival data were calculated more than 3 years after hepatic resection. We clearly demonstrated lower intraoperative blood loss (163 g vs 415 g, $P < 0.001$) and a smaller ratio of massive bleeding larger than 1,000 mL (6.4% vs 17.6%, $P < 0.001$). It is essential for CRLM patients undergoing hepatectomy to minimize blood loss. We have reported that substantial intraoperative blood loss can worsen OS for liver cancer patients after hepatectomy [45]. The CO₂ pneumoperitoneum is generally established at 10–14 mmHg, and this provides a fairly good control of back-bleeding during liver transection. Low central venous pressure (<5 mm Hg) should be used during LLR, as in open surgery [14]. Among other perioperative findings, we observed a shorter hospital stay (12 days vs 14 days, $P < 0.001$) and equivalent operation time, complication rate, transfusion rate, and R0 operation rate in LLR compared with OLR. Furthermore long-term RFS, OS, and DSS were comparable, and these results add support to previous reports.

Laparoscopic liver resection has been widely used for the treatment of malignant liver tumors instead of OLR [24]. Although we can assess the malignancy of CRLM using tumor size, tumor number, and the levels of serum tumor markers, it is difficult to evaluate the complexity of hepatic resection. Han and coworkers [13] demonstrated difficult tumor locations for LLR, and therefore we assessed this item in the present study. Practically, this variable was significantly different in the two groups, equaling however after PSM. In fact, the median operative time and the amount of intraoperative bleeding were significantly greater in the posterosuperior group than in the anterolateral group (data not shown). We have already identified important factors related to the complexity of hepatic resection, namely deep location and vascular proximity [46], but unfortunately data on these factors were not included in the current database. Lately, a novel difficulty scoring system for LLR was introduced [47]. This scoring system can be used to predict the difficulty of LLR from preoperative factors and to properly select patients according to the skill level of the surgeon.

Although OLR has been the golden standard procedure for CRLM, LLR has not proved to be a comparable surgical intervention. Specific concerns about the oncologic adequacy of laparoscopy in general include port site metastases, the trophic effect of pneumoperitoneum on malignant cells, and the inability to inspect the peritoneal cavity adequately when inspecting the liver [31, 48–51]. Therefore, we analyzed details of complications and postoperative recurrence. Morbidity rates and levels of complication were similar including no port site recurrences or seeding of malignant cells. We observed no specific

disadvantages regarding recurrence in LLR patients when we analyzed recurrence-free time from initial hepatic resection, and the number and size of initial recurrences. LLR included the Pure, HALS, and the Hybrid technique [12]. The independent role of these three approaches is not well known. A recent literature review demonstrated that there is insufficient evidence to conclude that any single approach is superior to the others, although HALS and the Hybrid technique are useful when dealing with difficulties associated with Pure LLR. Conversely, the need for these two methods, which can function as a bridge to Pure LLR, may be overcome with appropriate training [47, 52].

A problematic limitation was that this study was not an RCT. Although a well-designed PSM analysis was reported to be as accurate as an RCT [36], probable minimal confounding factors could have affected the results. Second, this study was investigated in the initial period of LLR usage for CRLM in Japan. The LLR to OLR ratio was 1: 5.3. The ratio of the Pure, HALS, and Hybrid approaches were 62%: 9%: 29%. The percent increase in LLR, was 16.9% between the first half and second half. The results might be modified with an increased number of LLR. Finally, in the propensity-matched cohort, median observation periods were different between the two procedures (LLR, 41.7 months vs OLR, 49.1 months). The sample size decreased after PSM, which could have affected the accuracy of recurrence and survival-estimated data. A total of 1,121 OLR patients were reduced to 513 patients after the PSM, which is caused by the small sample size of LLR group. One fifth of the LLR patients were excluded from the final analysis that might account for PSM selection bias. We can conclude from this PSM study that LLR can provide excellent perioperative benefits without compromising oncologic outcomes or long-term survival for patients with relatively early stage of CRLM. LLR should be considered to be a standard practice for selected patients with CRLM.

Acknowledgements We sincerely thank the patients who participated in this study and their families. We are indebted to the surgeons for their excellent collection and management of data and any other support for the Endoscopic Liver Surgery Study Group: Yasushi Hasegawa, Yoshinao Tanahashi, Etsuro Hatano, Osamu Itano, Yuichiro Otsuka, Naokazu Chiba, Tadashi Tsukamoto, Takanori Morikawa, Yutaka Takeda, Tetsuo Ikeda, Hiroshi Yoshida, Masayuki Ohta, Satoshi Matsumura, Mitsuo Shimada, Hiroshi Nakashima, Yasutsugu Takada, Masayuki Shiraiishi, Hirano Tadamichi, Chikaharu Sakata, Takashi Shirobe, and Masayasu Aikawa. We express our sincere appreciation for the Joint Committee of Liver Metastases Survey from Colorectal Cancer.

Conflict of interest Masafumi Nakamura has received lecture fees from Johnson & Johnson.

Appendix: author's affiliations

Toru Beppu and Hideo Baba, Department of Gastroenterological Surgery, Graduate School of Life Sciences, Kumamoto

University, Kumamoto, Japan; Go Wakabayashi and Takeshi Takahara, Department of Surgery, Iwate Medical University School of Medicine, Iwate, Japan; Kiyoshi Hasegawa and Norihiro Kokudo, Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; Naoto Gotohda and Masaru Konishi, Department of Hepatobiliary and Pancreatic Surgery, National Cancer Center Hospital East, Kashiwa, Chiba, Japan; Toru Mizuguchi and Koichi Hirata, Department of Surgery, Surgical Oncology and Science, Sapporo Medical University School of Medicine, Sapporo, Japan; Yutaka Takahashi and Masakazu Yamamoto, Department of Surgery, Institute of Gastroenterology, Tokyo Women's Medical University, Tokyo, Japan; Fumitoshi Hirokawa and Kazuhisa Uchiyama, Department of General and Gastroenterological Surgery, Osaka Medical College, Osaka, Japan; Nobuhiko Taniyai and Eiji Uchida, Department of Gastrointestinal Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan; Manabu Watanabe and Shinya Kusachi, Department of Surgery, Toho University Ohashi Medical Center, Tokyo, Japan; Masato Katou and Keiichi Kubota, Department of Gastroenterological Surgery, Dokkyo Medical University, Tochigi, Japan; Hiroaki Nagano and Masaki Mori, Department of Surgery, Osaka University Graduate School of Medicine, Suita, Osaka, Japan; Goro Honda and Keiichi Takahashi, Department of Surgery, Tokyo Metropolitan Cancer and Infectious Disease Center Komagome Hospital, Tokyo, Japan; Ken Kikuchi, Medical Quality Management Center, Kumamoto University Hospital, Kumamoto, Japan; Hiroaki Miyata, Department of Healthcare Quality Assessment, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; Masafumi Nakamura, Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; Hironori Kaneko, Department of Surgery, Toho University Faculty of Medicine, Tokyo, Japan; Hiroki Yamaue, Second Department of Surgery, Wakayama Medical University, School of Medicine, Wakayama, Japan; Masaru Miyazaki, Department of General Surgery, Chiba University Graduate School of Medicine, Chiba, Japan; Tadahiro Takada, Japanese Society of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Teikyo University School of Medicine, Tokyo, Japan.

References

- Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg.* 1999;230:309–18.
- Choti MA, Sitzmann JV, Tiburi MF, Sumetchotimetha W, Rangsin R, Schulick RD, et al. Trends in long-term survival following liver resection for hepatic colorectal metastases. *Ann Surg.* 2002;235:759–66.
- Mann CD, Metcalfe MS, Leopardi LN, Maddern GJ. The clinical risk score: emerging as a reliable preoperative prognostic index in hepatectomy for colorectal metastases. *Arch Surg.* 2004;139:1168–72.
- Cummings LC, Payes JD, Cooper GS. Survival after hepatic resection in metastatic colorectal cancer: a population-based study. *Cancer* 2007;109:718–26.
- Beppu T, Sakamoto Y, Hasegawa K, Honda G, Tanaka K, Kotera Y, et al. A nomogram predicting disease-free survival in patients with colorectal liver metastases treated with hepatic resection: multicenter data collection as a Project Study for Hepatic Surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. *J Hepatobiliary Pancreat Sci.* 2012;19:72–84.
- Aloia TA, Vauthey JN, Loyer EM, Ribero D, Pawlik TM, Wei SH, et al. Solitary colorectal liver metastasis: resection determines outcome. *Arch Surg.* 2006;141:460–6.
- Schiffman SC, Bower M, Brown RE, Martin RC, McMasters KM, Scoggins CR. Hepatectomy is superior to thermal ablation for patients with a solitary colorectal liver metastasis. *J Gastrointest Surg.* 2010;14:1881–6.
- Adam R, De Gramont A, Figueras J, Guthrie A, Kokudo N, Kunstlinger F, et al. of the EGOSLIM (Expert Group on OncoSurgery management of Liver Metastases) group. The oncosurgery approach to managing liver metastases from colorectal cancer: a multidisciplinary international consensus. *Oncologist.* 2012;17:1225–39.
- Beppu T, Miyamoto Y, Sakamoto Y, Imai K, Nitta H, Hayashi H, et al. Chemotherapy and targeted therapy for patients with initially unresectable colorectal liver metastases, focusing on conversion hepatectomy and long-term survival. *Ann Surg Oncol.* 2014;21Suppl 3:405–13.
- de Jong MC, Pulitano C, Ribero D, Strub J, Mentha G, Schulick RD, et al. Rates and patterns of recurrence following curative intent surgery for colorectal liver metastasis. An international multi-institutional analysis of 1669 patients. *Ann Surg.* 2009;250:440–48.
- Wicherts DA, de Haas RJ, Salloum C, Andreani P, Pascal G, Sotirov D, et al. Repeat hepatectomy for recurrent colorectal metastases. *Br J Surg.* 2013;100:808–18.
- Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I, et al. World Consensus Conference on Laparoscopic Surgery. The international position on laparoscopic liver surgery: The Louisville Statement, 2008. *Ann Surg.* 2009;250:825–30.
- Cho JY, Han HS, Yoon YS, Shin SH. Experiences of laparoscopic liver resection including lesions in the posterosuperior segments of the liver. *Surg Endosc.* 2008;22:2344–49.
- Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, Han HS, et al. Recommendations for laparoscopic liver resection: A report from the 2nd International Consensus Conference Held in Morioka. *Ann Surg.* 2015;261:619–29.
- Koffron AJ, Auffenberg G, Kung R, Abecassis M. Evaluation of 300 minimally invasive liver resections at a single institution: less is more. *Ann Surg.* 2007;246:385–92.
- Simillis C, Constantinides VA, Tekkis PP, Darzi A, Lovegrove R, Jiao L, et al. Laparoscopic versus open hepatic resections for benign and malignant neoplasma meta-analysis. *Surgery.* 2007;141:203–11.
- Nguyen KT, Marsh JW, Tsung A, Steel JJ, Gamblin TC, Geller DA. Comparative benefits of laparoscopic vs open hepatic resection: a critical appraisal. *Arch Surg.* 2011;146:348–56.
- Rao A, Rao G, Ahmed I. Laparoscopic or open liver resection? Let systematic review decide it. *Am J Surg.* 2012;204:222–31.
- Vanounou T, Steel JL, Nguyen KT, Tsung A, Marsh JW, Geller DA, et al. Comparing the clinical and economic impact of laparoscopic versus open liver resection. *Ann Surg Oncol.* 2010;17:998–1009.

20. Polignano FM, Quyn AJ, Sanjay P, Henderson NA, Tait IS. Totally laparoscopic strategies for the management of colorectal cancer with synchronous liver metastasis. *Surg Endosc.* 2012;26:2571–8.
21. Mala T, Edwin B, Gladhaug I, Fosse E, Søreide O, Bergan A, et al. A comparative study of the short-term outcome following open and laparoscopic liver resection of colorectal metastases. *Surg Endosc.* 2002;16:1059–63.
22. Castaing D, Vibert E, Ricca L, Azoulay D, Adam R, Gayet B. Oncologic results of laparoscopic versus open hepatectomy for colorectal liver metastases in two specialized centers. *Ann Surg.* 2009;250:849–55.
23. Kazaryan AM, Marangos IP, Rosok BI, Rosseland AR, Villanger O, Fosse E, et al. Laparoscopic resection of colorectal liver metastases: surgical and long-term oncologic outcome. *Ann Surg.* 2010;252:1005–12.
24. Nguyen KT, Laurent A, Dagher I, Geller DA, Steel J, Thomas MT, et al. Minimally invasive liver resection for metastatic colorectal cancer: a multi-institutional, international report of safety, feasibility, and early outcomes. *Ann Surg.* 2009;250:842–8.
25. Nguyen KT, Gamblin TC, Geller DA. World review of laparoscopic liver resection – 2,804 patients. *Ann Surg.* 2009;250:831–41.
26. Gueron AD, Aliyev S, Agcaoglu O, Aksoy E, Taskin HE, Aucejo F, et al. Laparoscopic versus open resection of colorectal liver metastasis. *Surg Endosc.* 2013;27:1138–43.
27. Topal H, Tiek J, Aerts R, Topal B. Outcome of laparoscopic major liver resection for colorectal metastases. *Surg Endosc.* 2012;26:2451–5.
28. Schiffman SC, Kim KH, Tsung A, Marsh JW, Geller DA. Laparoscopic versus open liver resection for metastatic colorectal cancer: A metaanalysis of 610 patients. *Surgery.* 2015;157:211–22.
29. Wei M, He Y, Wang J, Chen N, Zhou Z, Wang Z. Laparoscopic versus open hepatectomy with or without synchronous colectomy for colorectal liver metastasis: a meta-analysis. *PLoS One.* 2014;9:e87461.
30. Parks KR, Kuo YH, Davis JM, O'Brien B, Hagopian EJ. Laparoscopic versus open liver resection: a meta-analysis of long-term outcome. *HPB (Oxford).* 2014;16:109–18.
31. Cannon RM, Scoggins CR, Callender GG, McMasters KM, Martin RC 2nd. Laparoscopic versus open resection of hepatic colorectal metastases. *Surgery.* 2012;152:567–73.
32. de Angelis N, Eshkenazy R, Brunetti F, Valente R, Costa M, Disabato M, et al. Laparoscopic Versus Open Resection for Colorectal Liver Metastases: A Single-Center Study with Propensity Score Analysis. *J Laparoendosc Adv Surg Tech A.* 2015;25:12–20.
33. Lin Q, Ye Q, Zhu D, Wei Y, Ren L, Zheng P, et al. Comparison of minimally invasive and open colorectal resections for patients undergoing simultaneous R0 resection for liver metastases: a propensity score analysis. *Int J Colorectal Dis.* 2015;30:385–95.
34. D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med.* 1998;17:2265–81.
35. Austin PC. Statistical criteria for selecting the optimal number of untreated subjects matched to each treated subject when using many-to-one matching on the propensity score. *Am J Epidemiol.* 2010;172:1092–97.
36. Guo S, Fraser MW. Propensity score analysis: Statistical methods and applications. Sage Publications. 2014;11.
37. Lonjon G, Boutron I, Trinquart L, Ahmad N, Aim F, Nizard R, et al. Comparison of treatment effect estimates from prospective nonrandomized studies with propensity score analysis and randomized controlled trials of surgical procedures. *Ann Surg.* 2014;259:18–25.
38. Strasberg SM. Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. *J Hepatobiliary Pancreat Surg.* 2005;12:351–55.
39. Beppu T, Sakamoto Y, Hasegawa K, Honda G, Tanaka K, Kotera Y, et al. Optimal cut-off value for the number of colorectal liver metastases: a project study for hepatic surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. *J Hepatobiliary Pancreat Sci.* 2014;21:169–75.
40. Hayashi H, Beppu T, Okabe H, Kuroki H, Nakagawa S, Imai K, et al. Functional assessment versus conventional volumetric assessment in the prediction of operative outcomes after major hepatectomy. *Surgery.* 2015;157:20–6.
41. Otsuka Y, Kaneko H, Cleary SP, Buell JF, Cai X, Wakabayashi G. What is the best technique in parenchymal transection in laparoscopic liver resection? Comprehensive review for the clinical question on the 2nd International Consensus Conference on Laparoscopic Liver Resection. *J Hepatobiliary Pancreat Sci.* 2015;22:363–70.
42. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg.* 2009;250:187–96.
43. Hibi T, Cherqui D, Geller DA, Itano O, Kitagawa Y, Wakabayashi G. International Survey on Technical Aspects of Laparoscopic Liver Resection: a web-based study on the global diffusion of laparoscopic liver surgery prior to the 2nd International Consensus Conference on Laparoscopic Liver Resection in Iwate, Japan. *J Hepatobiliary Pancreat Sci.* 2014;21:737–44.
44. Wakabayashi G, Cherqui D, Geller DA, Han HS, Kaneko H, Buell JF. Laparoscopic hepatectomy is theoretically better than open hepatectomy: preparing for the 2nd International Consensus Conference on Laparoscopic Liver Resection. *J Hepatobiliary Pancreat Sci.* 2014;21:723–31.
45. Chikamoto A, Beppu T, Masuda T, Otao R, Okabe H, Hayashi H, et al. Amount of operative blood loss affects the long-term outcome after liver resection for hepatocellular carcinoma. *Hepatogastroenterology.* 2012;59:1213–16.
46. Beppu T, Hayashi H, Okabe H, Imai K, Nitta H, Masuda T, et al. Hybrid-including endoscopic versus open hepatic resection for patients with hepatocellular carcinoma meeting the Milan Criteria: a propensity case-matched analysis. *Anticancer Res.* 2015;35:1583–90.
47. Ban D, Tanabe M, Ito H, Otsuka Y, Nitta H, Abe Y, et al. A novel difficulty scoring system for laparoscopic liver resection. *J Hepatobiliary Pancreat Sci.* 2014;21:745–753.
48. Johnstone PA, Rohde DC, Swartz SE, Fetter JE, Wexner SD. Port site recurrences after laparoscopic and thoracoscopic procedures in malignancy. *J Clin Oncol.* 1996;14:1950–6.
49. Paolucci V, Schaeff B, Schneider M, Gutt C. Tumor seeding following laparoscopy: international survey. *World J Surg.* 1999;23:989–95.
50. Ishida H, Murata N, Yamada H, et al. Effect of CO₂ pneumoperitoneum on growth of liver micrometastases in a rabbit model. *World J Surg.* 2000;24:1004–8.
51. Gutt CN, Riemer V, Kim ZG, Erceg J, Lorenz M. Impact of laparoscopic surgery on experimental hepatic metastases. *Br J Surg.* 2001;88:371–5.
52. Hasegawa Y, Koffron AJ, Buell JF, Wakabayashi G. Approaches to laparoscopic liver resection: A meta-analysis of the role of hand-assisted laparoscopic surgery and the hybrid technique. *J Hepatobiliary Pancreat Sci.* 2015;22:335–41.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 Comparison of continuous background factors for LLR and OLR before and after PSM matching.

Fig. S1 Standardized differences before and after PSM. Open circle, before propensity matching; closed triangle, after propensity matching.

Multicenter comparative study of laparoscopic and open distal pancreatectomy using propensity score-matching

Masafumi Nakamura · Go Wakabayashi · Yoshihiro Miyasaka · Masao Tanaka · Takanori Morikawa · Michiaki Unno · Hiroshi Tajima · Yusuke Kumamoto · Sohei Satoi · Masanori Kwon · Hirochika Toyama · Yonson Ku · Hideyuki Yoshitomi · Satoshi Nara · Kazuaki Shimada · Takahide Yokoyama · Shinichi Miyagawa · Yoichi Toyama · Katsuhiko Yanaga · Tsutomu Fujii · Yasuhiro Kodera · Study Group of JHBPS and JSEPS · Yasuyuki Tomiyama · Hiroaki Miyata · Takeshi Takahara · Toru Beppu · Hiroki Yamaue · Masaru Miyazaki · Tadahiro Takada

Published online: 18 June 2015

© 2015 Japanese Society of Hepato-Biliary-Pancreatic Surgery

The author's affiliations are listed in the Appendix.

Correspondence to:
Masafumi Nakamura, Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan
e-mail: mnaka@surg1.med.kyushu-u.ac.jp

DOI: 10.1002/jhbp.268

Abstract

Background Laparoscopic distal pancreatectomy has been shown to be associated with favorable postoperative outcomes using meta-analysis. However, there have been no randomized controlled studies yet. This study aimed to compare laparoscopic and open distal pancreatectomy using propensity score-matching.

Methods We retrospectively collected perioperative data of 2,266 patients who underwent distal pancreatectomy in 69 institutes from 2006–2013 in Japan. Among them, 2,010 patients were enrolled in this study and divided into two groups, laparoscopic distal pancreatectomy and open distal pancreatectomy. Perioperative outcomes were compared between the groups using unmatched and propensity matched analysis.

Results After propensity score-matching, laparoscopic distal pancreatectomy was associated with favorable perioperative outcomes compared with open distal pancreatectomy, including higher rate of preservation of spleen and splenic vessels ($P < 0.001$); lower rates of intraoperative transfusion ($P = 0.020$), clinical grade of pancreatic fistula (International Study Group on Pancreatic Fistula grade B and C; $P < 0.001$), and morbidity ($P < 0.001$); and shorter hospital stay ($P = 0.001$), but a longer operative time ($P < 0.001$).

Conclusions Laparoscopic distal pancreatectomy was associated with more favorable perioperative outcomes than open distal pancreatectomy.

Keywords Laparoscopic distal pancreatectomy · Morbidity · Pancreatic fistula · Propensity score-matching

Introduction

Laparoscopic distal pancreatectomy (LDP) was first reported in 1996 by Gagner and Cuschieri [1, 2] and has since become common as a treatment method for benign pancreatic tumors due to the development of relevant surgical instruments and techniques. As LDP began to be widely performed, many retrospective studies and systematic reviews showed that LDP was not inferior to open distal pancreatectomy (ODP) in terms of short-term postoperative outcomes and that LDP was associated with a shorter hospital stay compared with ODP [3–6]. Furthermore, some systematic reviews with meta-analysis showed that LDP is associated with better short-term postoperative outcomes in terms of postoperative pain, recovery time, length of hospital stay, rate of postoperative pancreatic fistula (POPF), and postoperative morbidity [3, 5–8]. However, these systematic reviews using meta-analysis did not

include any randomized controlled trials (RCTs), and thus, selection bias in treatment methods may have influenced their results [3, 5, 8–10].

Because LDP is safe and associated with favorable postoperative outcomes as described above, LDP is now a common technique for benign tumors [11]. Therefore, a RCT comparing LDP to ODP is challenging today. We organized a nationwide retrospective collection of perioperative data from patients who underwent LDP or ODP for benign tumors. Instead of a RCT, the pooled data were subjected to propensity score-matching (PSM) for comparing the outcomes of LDP and ODP [12]. The aim of this study was to establish evidence concerning postoperative outcomes after LDP for benign tumors.

Methods

Study selection

We conducted a retrospective cohort study as a project of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JHBPS) and collected perioperative data for 2,266 patients who underwent distal pancreatectomy from 2006–2013 at 69 institutes that participated in JHBPS and the Japanese Society for Endoscopic Pancreatic Surgery. The inclusion criterion was a preoperative diagnosis of a benign or low-grade malignant tumor of the pancreas, and thus, patients with preoperative diagnosis of an invasive pancreatic cancer were excluded from this study. Data were treated based on intention-to-treat concerning diagnosis and surgical method. According to the criteria, 145 patients with preoperative diagnosis as an invasive cancer, and a patient with insufficient data, were excluded from our study. Eventually, 2,120 patients were enrolled. The numbers of patients who underwent the different surgical procedures were as follows: ODP ($n=1,108$), pure LDP (P-LDP; $n=770$), hand-assisted LDP (HA-LDP; $n=132$), and hybrid-distal pancreatectomy (HDP; $n=110$). HDP patients were excluded from the analysis, because its definition is vague. The remaining 2,010 patients were divided into two groups, ODP ($n=1,108$) and LDP ($n=902$).

Pancreatic fistula and postoperative morbidity

Postoperative pancreatic fistula was diagnosed by the International Study Group of Pancreatic Fistula (ISGPF) and evaluated according to the following criteria: persistent drainage (>3 weeks), signs of infection, readmission within 1 month, or fluid collection with elevated drain amylase levels (>3 times the upper limit of normal serum amylase level), as previously described [13]. The definition of postoperative morbidity was a postoperative event of grade

III–V of Clavien–Dindo classification or POPF of grade B or C [14, 15].

Statistical analysis

To determine the efficacy of treatment and to reduce the effect of selection bias, propensity score analysis was performed using the following algorithm. Possible confounders were chosen for their potential association with the outcome based on clinical knowledge. A propensity score was estimated using a logistic regression model using the following 14 relevant variables: age, gender, body mass index (BMI), maximum tumor size, locations of tumors, prior abdominal surgery, comorbidity, hemoglobin, albumin, carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), pancreatitis other than obstructive pancreatitis caused by the tumor, obstructive pancreatitis caused by the tumor, and combined resection of other organs. Propensity scores were matched using a caliper width of 0.25 multiplied by the standard deviation of values that was calculated by a logistic regression model. One patient who underwent laparoscopic surgery was matched to one patient who underwent laparotomy using a greedy nearest-neighbor matching algorithm without replacement. We used the receiver operating characteristic (ROC) and area under the curve (AUC) to measure the balance of covariates. Within this matched cohort, the AUC was 0.54 ($P=0.009$, 95% confidence interval [CI]: 0.510–0.569) calculated from the ROC curve. Continuous variables were compared by t -tests, and categorical variables were compared by χ^2 test. A P -value < 0.05 was considered to be significant. All analyses described above were performed using SPSS software (version 22, SPSS, Chicago, IL, USA).

Results

Patient characteristics

Patient characteristics before and after PSM are shown in Table 1. Out of 902 patients in the LDP group, in 58 patients operation was converted to ODP and was counted as LDP based on intention-to-treat. In addition, 13 out of 14 factors that were important for selecting the operative method were significantly different between the LDP and ODP groups before PSM. The factors showing differences were: age, gender, BMI, tumor size, tumor location, prior abdominal surgery, comorbidity, hemoglobin, albumin, CEA, CA19-9, pancreatitis, and combined resection of other organs. Finally, 1,458 out of 2,010 enrolled patients remained, and none of the 14 factors related to patient characteristics showed a statistical difference between the LDP and ODP groups after PSM (Table 1).

Table 1 Patient characteristics

	Before PSM (<i>n</i> = 2,010)			After PSM (<i>n</i> = 1,458)		
	ODP (1,108)	LDP (902)	<i>P</i>	ODP (729)	LDP (729)	<i>P</i>
Age (years) ^c	61 ± 15	57 ± 16	<0.001*	59 ± 15	58 ± 16	0.771
Gender (male/female)	502/606	321/581	<0.001*	294/435	269/460	0.179
Body mass index (kg/m ²) ^c	22.1 ± 3.7	22.5 ± 5.1	0.038*	22.2 ± 3.7	22.4 ± 3.7	0.280
Tumor size (mm) ^c	39 ± 32	35 ± 25	0.001*	35 ± 28	35 ± 26	0.938
Tumor location Body/tail/body-tail (%)	61.1/37.2/1.7	47.6/52.3/0.1	<0.001*	54.6/44.3/1.1	53.4/46.5/0.1	0.480
Prior abdominal surgery (%)	32.5	23.4	<0.001*	27.6	26.1	0.497
Comorbidity (%)	51.9	41.4	<0.001*	45.5	45.7	0.916
Hb < 10.0 g/dL (%)	5.9	3.4	0.008*	4.6	4.0	0.607
ALB < 3.5 g/dL (%)	8.7	4.6	<0.001*	5.2	5.1	0.915
Elevated CEA (%)	11.9	8.5	0.015*	9.8	8.9	0.560
Elevated CA19-9 (%)	14.3	9.5	0.002*	8.4	10.2	0.258
Pancreatitis (%) ^a	14.0	8.0	<0.001*	9.5	8.5	0.521
Obstructive pancreatitis (%) ^b	4.3	3.4	0.181	3.3	3.6	0.733
Combined resection of other organs (%)	24.2	11.0	<0.001*	15.6	13.1	0.175

ALB albumin, Hb hemoglobin, LDP laparoscopic distal pancreatectomy, ODP open distal pancreatectomy, PSM propensity score matching. Elevated CEA and CA19-9: Increased value of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) beyond the standards of institutes

* Indicates statistical significance ($P < 0.05$)

^a Pancreatitis except obstructive pancreatitis by tumor

^b Obstructive pancreatitis caused by tumor

^c Values are mean ± standard deviation

Perioperative outcomes

The matched cohort was evaluated for differences in perioperative outcomes between LDP and ODP (Tables 2 and 3), and the results are shown in Table 2 with the results of an unmatched analysis. LDP showed several favorable outcomes compared with ODP, except for operative time (319.2 and 261.4 min for LDP and ODP, respectively; $P < 0.001$). The preservation rates of the spleen (29.9% vs 13.2%; $P < 0.001$) and splenic vessels (25.7% vs 12.3%; $P < 0.001$) were higher in the LDP group than those in the ODP group. The intraoperative transfusion rate was significantly lower in LDP than in ODP (4.0% vs 6.8%; $P = 0.020$, odds ratio = 0.574 with 95% CI = 0.358–0.919). The clinical grade of pancreatic fistula (POPF-B.C) was less in the LDP group than in the ODP group (18.4% vs 28.2%; $P < 0.001$, odds ratio = 0.575 with 95% CI = 0.448–0.739). The overall morbidity rate was less for LDP than for ODP (24.0% vs 32.5%; $P < 0.001$, odds ratio = 0.654 with 95% CI = 0.520–0.824). Details of intraoperative complications and overall morbidity are shown in Table 4. LDP was associated with a shorter hospital stay compared with ODP (18.8 vs 23.2 days; $P = 0.001$). No significant differences were observed in the 30-day and 90-day mortality rates between the two groups. Although the POPF-A.B.C appeared to be different between the groups, with PSM no statistical difference was observed.

Discussion

Although no RCT comparing LDP with ODP has been published, LDP rapidly has become a common treatment for benign tumors [11]. Our study included the largest number of patients in a comparative study of LDP with ODP out of all studies that we could find on PubMed [16]. The groups matched by propensity scores were compared for postoperative factors. LDP showed several favorable results, such as less blood loss; lower rates of transfusion, POPF-B.C, and overall morbidity; and shorter hospital stay. Odds ratios of LDP to ODP for transfusion, POPF-B.C, and morbidity were 0.574, 0.575, and 0.654, respectively. Our observation that LDP showed favorable short-term outcomes may accelerate the spread of LDP.

When we compared patient characteristics between the LDP and ODP groups, 13 out of 14 factors related to patient characteristics showed significant differences before PSM. As expected, patients who underwent LDP tended to be healthy young women, and operations were expected to be simple without prior operation or pancreatitis as shown in Table 1.

Most of the systematic reviews and independent comparative studies have coincided with each other regarding the non-inferiority of LDP in terms of postoperative outcomes and the superiority of LDP with respect to hospital stay and transfusion rate [3, 5, 7, 8]. However, there is controversy about

Table 2 Perioperative outcomes

	Before PSM (n = 2,010)			After PSM (n = 1,458)		
	ODP (1,108)	LDP (902)	P	ODP (729)	LDP (729)	P
Operative time (min) [§]	268 ± 115	316 ± 127	<0.001*	261 ± 119	319 ± 129	<0.001*
Estimated blood loss (g)	568 ± 806	243 ± 388	<0.001*	499 ± 740	254 ± 384	<0.001*
Drain amylase (IU/L) [§]	8066 ± 15983	8085 ± 13783	0.979	9324 ± 17591	8084 ± 14662	0.181
Days of drainage [§]	14.6 ± 18.1	12.5 ± 34.4	0.086	15.7 ± 19.3	12.6 ± 37.7	0.052
Day of meal intake [§]	5.6 ± 5.2	5.5 ± 6.1	0.483	5.6 ± 5.1	5.3 ± 5.8	0.392
Hospital stay (days) [§]	23.3 ± 17.7	18.9 ± 14.4	<0.001*	23.2 ± 18.8	18.8 ± 14.7	0.001*
Preservation of spleen (%)	10.6	32	<0.001*	13.2	29.9	<0.001*
Preservation of splenic vessels (%)	9.7	27.5	<0.001*	12.3	25.7	<0.001*
Intraoperative transfusion (%)	10.0	3.9	<0.001*	6.8	4.0	0.020*
Intraoperative complication (%)	5.1	4.1	0.29	4.0	4.7	0.527
POPF-A,B,C (%)	59.7	66.2	0.003*	64.0	65.8	0.489
POPF-B,C (%)	26.7	18.2	<0.001*	28.2	18.4	<0.001*
Overall morbidity (%)	31.6	23.6	<0.001*	32.5	24.0	<0.001*
30-day mortality (yes/no)	2/1106	1/901	0.577	0/729	1/728	0.500
90-day mortality (yes/no)	3/1105	2/900	0.596	1/728	2/727	0.500

LDP laparoscopic distal pancreatectomy, ODP open distal pancreatectomy, POD postoperative day, POPF-A,B,C postoperative pancreatic fistula of grade A, B and C, POPF-B,C postoperative pancreatic fistula of grade B and C, PSM propensity score matching.

* Indicates statistical significance ($P < 0.05$).

§ Values are mean ± standard deviation, drain amylase was measured on 1POD.

Table 3 Odds ratios for postoperative pancreatic fistula (POPF) and morbidity after propensity score-matching (PSM)

	Odds ratio (LDP/ODP)	95% confidence interval	P
Intraoperative transfusion	0.574	0.358 to 0.919	0.020*
POPF-BC	0.575	0.448 to 0.739	<0.001*
Overall morbidity	0.654	0.520 to 0.824	<0.001*

LDP laparoscopic distal pancreatectomy, ODP open distal pancreatectomy, POPF-B,C postoperative pancreatic fistula of grade B and C, PSM propensity score matching.

* Indicates statistical significance ($P < 0.05$).

the superiority of POPF and morbidity [3, 5, 7–10, 17]. Interestingly, we showed that LDP were associated with significantly higher POPF-A,B,C than ODP before PSM, but the difference disappeared after PSM. This meant that some of the 13 factors related to patient characteristics, which were significantly different between the LDP and ODP groups, accounted for the difference in the rate of POPF-A,B,C. Similar biases may have accounted for the difference in the rate of POPF between studies.

In our study, patients undergoing LDP showed a lower rate of POPF-B,C than patients undergoing ODP before and after PSM. There are some possible factors that may be responsible

Table 4 Details of intraoperative complications and overall morbidity

	Before PSM		After PSM	
	ODP	LDP	ODP	LDP
Intraoperative complication				
Bleeding	46	33	23	31
Injury of other organs	5	1	3	1
Miscellaneous	5	3	3	2
Postoperative morbidity*				
POPF-B,C	296	164	237	134
Intra-abdominal abscess	31	24	16	22
Delayed gastric emptying	9	5	6	5
Bleeding	5	12	4	10
Respiratory failure	5	1	2	1
Wound infection	2	3	2	2
Miscellaneous	56	30	38	21

LDP laparoscopic distal pancreatectomy, ODP open distal pancreatectomy, POPF-B,C postoperative pancreatic fistula of grade B and C, PSM propensity score matching.

* Some patients had more than one postoperative event.

for the superiority of LDP in terms of POPF-B,C. One possible factor is the difference in methods used for transecting the pancreas. However, a previous study reported that the major transection methods for ODP and LDP, hand-sewn closure and stapling, respectively, did not cause differences in POPF and morbidity [18]. This meant that the ability to seal the

pancreatic stump in LDP and ODP may be comparable. This idea was supported by our data that the drain amylase concentration on the first postoperative day was comparable between the LDP and ODP groups. Meanwhile, infection is one of the key factors for deteriorated POPF [19], and the infection risk is lower with LDP compared to ODP [3]. This could be one explanation for the decrease in POPF among patients undergoing LDP.

The operative time did not differ between the LDP and ODP groups in most of the meta-analysis, but LDP was associated with a significantly longer operative time than ODP in our study. This may be a result of the settings for matching factors. We set the rate of preservation of spleen and splenic vessels as a perioperative outcome, because we did not have data concerning the rate of intent to preserve them. It appeared that LDP had significantly higher rates for these factors. Methods with the preservation of the spleen and splenic vessels tend to require more time than methods without preservation [20–22]. Therefore, we speculated that LDP required more time because of the high rate of these preservation methods. Another reason may be the inclusion of data from institutes that were not high volume centers. Most previous reports from single centers were usually from high volume centers that were familiar with LDP, and surgeons at low volume institutes may still be in the learning curve for LDP [23, 24].

A limitation of our study is that PSM will not correct biases from unmeasured confounders. However, it is still useful to evaluate a treatment method more precise than conventional retrospective studies [12, 25].

In conclusion, LDP was associated with several favorable perioperative outcomes, particularly low rates of POPF and morbidity, in a large number of patients with PSM. However, we analyzed short-term outcomes exclusively in this study. We need to evaluate long-term prognosis after LDP even for benign and low grade malignant tumors before setting LDP as a first line method of resection for pancreatic body tumors.

Acknowledgments We thank Mrs Yuko Tanaka for her contribution to data collection and skillful technical assistance. Members of the Study Group of the Japanese Society of Hepato-Biliary-Pancreatic Surgery and the Japanese Society for Endoscopic Pancreatic Surgery are Drs. Hisatoshi Nakagawara, Eiji Uchida, Tamotsu Kuroki, Manabu Kawai, Takeaki Ishizawa, Toshihiro Okada, Yasunaru Sakuma, Hisashi Ikoma, Satoshi Yamamoto, Hiroshi Yokomizo, Naoto Gotohda, Koji Amaya, Akihiro Cho, Yukihiro Yokoyama, Daisuke Kawaguchi, Keinosuke Ishido, Yuichi Nagakawa, Akira Umemura, Masanao Kurata, Akihiro Takai, Masayuki Ohta, Yoshiaki Ohmura, Masaji Hashimoto, Norihiro Sato, Jiro Ohuchida, Masanobu Usui, Teruhisa Sakamoto, Hiroshi Nakashima, Shinjiro Tomiyasu, Minoru Kitago, Tadashi Tsukamoto, Keiichi Okano, Hironori Kaneko, Tsunehiko Maruyama, Eiichi Tanaka, Kenichiro Araki, Masahiro Ito, Tomokazu Kusano, Masato Yamazaki, Tomoyoshi Okamoto, Hiroshi Uchinami, Yoshiyuki Sasaki, Hiroki Sunagawa, Keiichi Suzuki, Takanori Sakaguchi, Yoshitaro Shindo, Kosei Maemura, Yasunari Kawabata, Shoji Kubo,

Akira Chikamoto, Kenji Kobayashi, Hiroki Mizukami, Yoshito Iida, Hideo Miyake, Kyoichi Takaori, Tetsuo Ikeda, Hiromichi Kawaida, Michihiro Maruyama, Kijuro Takanishi, Toshiyuki Natsume, Nobumi Tagaya, Fumiaki Kishihara, and Masaki Tokumo.

Conflict of interest Masafumi Nakamura has received a teaching fee from Johnson & Johnson. Masao Tanaka has received research funding from Covidien Japan and Johnson & Johnson, and has received honorarium from Covidien Japan. Yasuhiro Kodera has received grants from Taiho Pharmaceutical Company, Chugai Pharmaceutical Company, Pfizer, Eli Lilly Japan, Bristol Meyers Squib, Otsuka Pharmaceutical Factory, Takeda Pharmaceutical Company Ltd, Eisai, Yakult, Daiichi Sankyo, Mitsubishi, Tanabe Pharma, Merck and Shionogi.

Appendix: authors' affiliations

Masafumi Nakamura, Department of Digestive Surgery, Kawasaki Medical School, Kurashiki, Japan; Masafumi Nakamura, Yoshihiro Miyasaka and Masao Tanaka, Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; Go Wakabayashi and Takeshi Takahara, Department of Surgery, Iwate Medical University School of Medicine, Morioka, Japan; Takanori Morikawa and Michiaki Unno, Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan; Hiroshi Tajima and Yusuke Kumamoto, Department of Surgery, Kitasato University School of Medicine, Sagami, Japan; Sohei Satoi and Masanori Kwon, Department of Surgery, Kansai Medical University, Hirakata, Japan; Hirochika Toyama and Yonson Ku, Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan; Hideyuki Yoshitomi and Masaru Miyazaki, Department of General Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan; Satoshi Nara and Kazuaki Shimada, Hepatobiliary and Pancreatic Surgery Division, National Cancer Center Hospital, Tokyo, Japan; Takahide Yokoyama and Shinichi Miyagawa, First Department of Surgery, Shinshu University School of Medicine, Matsumoto, Japan; Yoichi Toyama and Katsuhiko Yanaga, The Jikei University School of Medicine, Tokyo, Japan; Tsutomu Fujii and Yasuhiro Kodera, Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, Japan; Study Group of JHBPS and JSEPS, JHBPS; Japanese Society of Hepato-Biliary-Pancreatic Surgery, JSEPS; Japanese Society for Endoscopic Pancreatic Surgery. Members of the study group are listed in acknowledgement; Yasuyuki Tomiyama, Department of Hepatology and Pancreatology, Kawasaki Medical School, Kurashiki, Japan; Hiroaki Miyata, Department of Healthcare Quality Assessment, Graduate School of Medicine, The

University of Tokyo, Tokyo, Japan; Toru Beppu, Department of Gastroenterological Surgery, Graduate School of Life Sciences, Kumamoto University, Kumamoto, Japan; Hiroki Yamaue, Second Department of Surgery, School of Medicine, Wakayama Medical University, Wakayama, Japan; Tadahiro Takada, Department of Surgery, Teikyo University School of Medicine, Tokyo, Japan

References

- Cuschieri A, Jakimowicz JJ, van Spreuwel J. Laparoscopic distal 70% pancreatectomy and splenectomy for chronic pancreatitis. *Ann Surg.* 1996;223:280–5.
- Gagner M, Pomp A, Herrera MF. Early experience with laparoscopic resections of islet cell tumors. *Surgery.* 1996;120:1051–4.
- Venkat R, Edil BH, Schulick RD, Lidor AO, Makary MA, Wolfgang CL. Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity compared to the open technique: a systematic review and meta-analysis. *Ann Surg.* 2012;255:1048–59.
- DiNordia J, Schrope BA, Lee MK, Reavey PL, Rosen SJ, Lee JA, et al. Laparoscopic distal pancreatectomy offers shorter hospital stays with fewer complications. *J Gastrointest Surg.* 2010;14:1804–12.
- Nakamura M, Nakashima H. Laparoscopic distal pancreatectomy and pancreatoduodenectomy: is it worthwhile? A meta-analysis of laparoscopic pancreatectomy. *J Hepatobiliary Pancreat Sci.* 2013;20:421–8.
- Aly MY, Tsutsumi K, Nakamura M, Nakamura M, Sato N, Takahata S, et al. Comparative study of laparoscopic and open distal pancreatectomy. *J Laparoendosc Adv Surg Tech A.* 2010;20:435–40.
- Nigri GR, Rosman AS, Petrucciani N, Fancellu A, Pisano M, Zorcolo L, et al. Metaanalysis of trials comparing minimally invasive and open distal pancreatectomies. *Surg Endosc.* 2011;25:1642–51.
- Jusoh AC, Ammori BJ. Laparoscopic versus open distal pancreatectomy: a systematic review of comparative studies. *Surg Endosc.* 2012;26:904–13.
- Jin T, Altaf K, Xiong JJ, Huang W, Javed MA, Mai G, et al. A systematic review and meta-analysis of studies comparing laparoscopic and open distal pancreatectomy. *HPB (Oxford).* 2012;14:711–24.
- Pericleous S, Middleton N, McKay SC, Bowers KA, Hutchins RR. Systematic review and meta-analysis of case-matched studies comparing open and laparoscopic distal pancreatectomy: is it a safe procedure? *Pancreas.* 2012;41:993–1000.
- Abu Hilal M, Takhar AS. Laparoscopic left pancreatectomy: current concepts. *Pancreatol.* 2013;13:443–8.
- Lonjon G, Boutron I, Trinquart L, Ahmad N, Aim F, Nizard R, et al. Comparison of treatment effect estimates from prospective nonrandomized studies with propensity score analysis and randomized controlled trials of surgical procedures. *Ann Surg.* 2014;259:18–25.
- Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery.* 2005;138:8–13.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240:205–13.
- Casadei R, Ricci C, Pezzilli R, Calculli L, D'Ambra M, Taffurelli G, et al. Assessment of complications according to the Clavien-Dindo classification after distal pancreatectomy. *JOP.* 2011;12:126–30.
- de Rooij T, Jilesen AP, Boerma D, Bonsing BA, Bosscha K, van Dam RM, et al. A nationwide comparison of laparoscopic and open distal pancreatectomy for benign and malignant disease. *J Am Coll Surg Mar.* 2015;220:263–270.e261.
- Mehrabi A, Hafezi M, Arvin J, Esmaeilzadeh M, Garoussi C, Emami G, et al. A systematic review and meta-analysis of laparoscopic versus open distal pancreatectomy for benign and malignant lesions of the pancreas: it's time to randomize. *Surgery.* 2015;157:45–55.
- Diener MK, Seiler CM, Rossion I, Kleeff J, Glanemann M, Butturini G, et al. Efficacy of stapler versus hand-sewn closure after distal pancreatectomy (DISPACT): a randomised, controlled multicentre trial. *Lancet.* 2011;377:1514–22.
- Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R, et al. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. *Ann Surg.* 2006;244:1–7.
- Nakamura M, Nagayoshi Y, Kono H, Mori Y, Ohtsuka T, Takahata S, et al. Lateral approach for laparoscopic splenic vessel-preserving distal pancreatectomy. *Surgery.* 2011;150:326–31.
- Matsushima H, Kuroki T, Adachi T, Kitasato A, Hirabaru M, Hidaka M, et al. Laparoscopic spleen-preserving distal pancreatectomy with and without splenic vessel preservation: the role of the Warsaw procedure. *Pancreatol.* 2014;14:530–5.
- Yu X, Li H, Jin C, Fu D, Di Y, Hao S, et al. Splenic vessel preservation versus Warsaw's technique during spleen-preserving distal pancreatectomy: a meta-analysis and systematic review. *Langenbecks Arch Surg.* 2015;400:183–91.
- Braga M, Ridolfi C, Balzano G, Castoldi R, Pecorelli N, Di Carlo V. Learning curve for laparoscopic distal pancreatectomy in a high-volume hospital. *Updates Surg.* 2012;64:179–83.
- Ricci C, Casadei R, Buscemi S, Taffurelli G, D'Ambra M, Pacilio CA, et al. Laparoscopic distal pancreatectomy: what factors are related to the learning curve? *Surg Today.* 2015;45:50–6.
- Glynn RJ, Schneeweiss S, Stürmer T. Indications for Propensity Scores and Review of Their Use in Pharmacoepidemiology. *Basic Clin Pharmacol Toxicol.* 2006;98:253–9.



Effects of body mass index (BMI) on surgical outcomes: a nationwide survey using a Japanese web-based database

Motonari Ri¹ · Hiroaki Miyata² · Susumu Aikou¹ · Yasuyuki Seto¹ · Kohei Akazawa³ · Masahiro Takeuchi⁴ · Yoshiro Matsui⁵ · Hiroyuki Konno⁶ · Mitsukazu Gotoh⁶ · Masaki Mori⁶ · Noboru Motomura⁷ · Shinichi Takamoto⁷ · Yoshiki Sawa⁸ · Hiroyuki Kuwano⁹ · Norihiro Kokudo¹⁰

Received: 12 June 2015 / Accepted: 10 July 2015 / Published online: 12 August 2015
© Springer Japan 2015

Abstract

Purpose To define the effects of body mass index (BMI) on operative outcomes for both gastroenterological and cardiovascular surgery, using the National Clinical Database (NCD) of the Japanese nationwide web-based database.

Methods The subjects of this study were 288,418 patients who underwent typical surgical procedures between January 2011 and December 2012. There were eight gastroenterological procedures, including esophagectomy, distal gastrectomy, total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy of >1 segment excluding the lateral segment, pancreaticoduodenectomy, and surgery for acute diffuse peritonitis ($n = 232,199$); and five cardiovascular procedures, including aortic valve replacement, total arch replacement (TAR), descending thoracic aorta replacement (descending TAR), and on- or off-pump coronary artery bypass grafting ($n = 56,219$). The relationships

of BMI with operation time and operative mortality for each procedure were investigated, using the NCD.

Results Operation times were longer for patients with a higher BMI. When a BMI cut-off of 30 was used, the operation time for obese patients was significantly longer than that for non-obese patients, for all procedures except esophagectomy ($P < 0.01$). The mortality rate based on BMI revealed a U-shaped distribution, with both underweight and obese patients having high mortality rates for almost all procedures.

Conclusions This Japanese nationwide study provides solid evidence to reinforce that both obesity and excessively low weight are factors that impact operative outcomes significantly.

Keywords National clinical database · Nationwide web-based database · Body mass index · Operation time · Operative mortality

On behalf of the Japan Surgical Society.

✉ Yasuyuki Seto
seto-tyk@umin.ac.jp

¹ Department of Gastrointestinal Surgery, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

² National Clinical Database (NCD), Tokyo, Japan

³ Department of Medical Informatics, Niigata University Medical and Dental Hospital, Niigata, Japan

⁴ Department of Clinical Medicine, School of Pharmacy, Kitasato University, Kanagawa, Japan

⁵ Department of Cardiovascular and Thoracic Surgery, Hokkaido University Graduate School of Medicine, Hokkaido, Japan

⁶ The Japanese Society of Gastroenterological Surgery, Tokyo, Japan

⁷ Japan Cardiovascular Surgery Database Organization, Tokyo, Japan

⁸ Department of Cardiovascular Surgery, Osaka University of Medicine, Osaka, Japan

⁹ Department of General Surgical Science, Graduate School of Medicine, Gunma University, Gunma, Japan

¹⁰ Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Table 1 Summary of past studies on the effect of body mass index on surgical outcomes

Year	References	<i>n</i>	Disease	Operation	BMI cut-off values	Operation time (min) <i>P</i> value	Mortality (%) <i>P</i> value
2013	Bhayani et al. [7]	794	–	Subtotal or total esophagectomy	18.5–25 vs. 35≤	316 vs. 308 n.s.	3.3 vs. 2.3 ns
2013	Sugimoto et al. [8]	216	Gastric cancer	Laparoscopic distal gastrectomy	25> vs. 25≤	200 vs. 212 0.005	0 vs. 0 ns
2014	Makino et al. [9]	152	Colon cancer	Laparoscopic colectomy	30> vs. 30≤	157 vs. 182 0.008	0 vs. 0 ns
2012	Saunders et al. [10]	403	–	Liver resection	18.5–24.9 vs. 40≤	306 vs. 402 ns	6 vs. 27 0.05
2014	El Nakeeb et al. [11]	471	Some	Pancreaticoduodenectomy	25> vs. 25≤	300 vs. 321 0.003	0.8 vs. 7.1 0.001
2012	Zdichavsky et al. [12]	596	Some	Laparoscopic cholecystectomy	30> vs. 30≤	73.5 vs. 87 <0.001	–
2011	Alam et al. [13]	13,115	–	Coronary artery bypass graft	30> vs. 30≤	39.3 vs. 41.7* <0.0001	3.7 vs. 2.9 ns
2012	Smith et al. [14]	1066	Aortic stenosis	Aortic valve replacement	25> vs. 25–30 vs. 30<	72.9 vs. 74.9 vs. 76.5** ns	5.6 vs. 2.8 vs. 4.5 ns

BMI body mass index

* Aortic clamp time, ** cross-clamp time

Introduction

With the proportion of obese people in world populations increasing, obesity-related illnesses have become a major concern globally [1]. The World Health Organization (WHO) has documented that 34 % of adult men and 35 % of adult women have a body mass index (BMI) of more than 25, and that 10 % of adult men and 14 % of adult women worldwide are obese (BMI ≥ 30) [2]. In the United States, 34.9 % of adults are obese [3]. Japan is no exception to this trend, with a National Health and Nutrition Survey (2012) conducted by the Ministry of Health, Labour and Welfare revealing that 29.1 % of adult men and 19.4 % of adult women have a BMI of more than 25. A rising BMI and a growing obese population in Japan have been reported, especially among men, as well as middle-aged and older women [4–7]. Although there have been a number of studies on the relationship between obesity and operative outcomes, their conclusions are inconsistent (Table 1) [8–15]. Moreover, many of these studies were performed at individual institutions and there have been no large-scale surveys comparing different surgical areas. Ultimately, it has not yet been established whether obesity adversely affects operative outcomes, such as the operation time and risk. Thus, we conducted a cross-sectional investigation of the effects of BMI on operation time and operative mortality for both gastroenterological and cardiovascular surgery, using a Japanese nationwide database.

Methods

The nationwide database system

In January 2011, Japan's National Clinical Database (NCD) became accessible on-line, with the cooperation of some of the nation's surgical associations. The NCD is a large-scale nationwide database, in which data from over 1,200,000 surgical cases were collected from more than 3500 hospitals in 2011. The information about operations performed nationwide was registered in the NCD by data management departments from the participating institutions. The data were evaluated annually using a web-based data management system to assure data traceability. This system also validated data consistency by randomly inspecting the participating institutions. Several clinical studies conducted by various societies have used the NCD data [16–18].

Patients

We analyzed data from a total 288,418 patients who underwent a typical procedure in the areas of gastroenterological and cardiovascular surgery between 1 January 2011 and 31 December 2012. There were 13 procedures in total: esophagectomy (Eso), distal gastrectomy (DG), total gastrectomy (TG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy of more than one segment apart from the lateral segment (Hx),

pancreaticoduodenectomy (PD), surgery for acute diffuse peritonitis (ADP), aortic valve replacement (AVR), total arch replacement (TAR), descending thoracic aorta replacement (descending TAR), coronary artery bypass graft (CABG) on-pump, and CABG off-pump. Patients who did not consent to their data being used were excluded from this analysis. Records with missing data for age, sex, or status at postoperative day (POD) 30 were also excluded, as were data related to patients with a BMI of less than 10 or over 50 as these values were obviously erroneous.

Study outcomes

The three outcomes examined using the NCD were BMI, operation time, and operative mortality. BMI is calculated as weight (in kilograms) divided by the square of height (in meters). Operative mortality included all deaths occurring within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), or after hospital discharge (within 30 days after surgery). We evaluated influences of stratified BMI on operation time and operative mortality.

Statistical analyses

All statistical analyses were conducted using SPSS (version 20). We performed univariate comparisons of BMI and operation time, using the unpaired Student's *t* test and Chi-square test. A *P* value of 0.05 was considered significant.

Results

Table 2 summarizes the backgrounds of each procedure. There were 232,199 patients undergoing 1 or more of 8 gastroenterological surgery procedures and 56,219 patients undergoing 1 or more of 5 cardiovascular surgery procedures.

BMI distribution

Figure 1 shows the BMI distribution of all the patients whose data were analyzed. Approximately 60 % of the procedures (61.2–69.9 %) were performed on patients with a normal physique, with a BMI of 18.5–25. Of the remaining patients, 2.6 % were obese, 20.3 % were overweight, and 13.4 % were underweight. There were differences in BMI distributions between patients undergoing gastroenterological and cardiovascular procedures. The largest category of patients undergoing gastroenterological surgery had a BMI of 18.5–22, and the largest category of those undergoing cardiovascular surgery had a BMI of 22–25. The proportion of overweight patients (with a BMI of 25–30) among those

Table 2 Background parameters

Operation	Number	Sex (male/female)	Age (mean ± SD)
Eso	10,825	9124/1701	66.1 ± 9.3
DG	63,650	42,438/21,212	69.1 ± 11.5
TG	37,817	27,877/9940	69.0 ± 11.0
RHC	37,750	18,878/18,872	71.7 ± 12.1
LAR	33,217	21,436/11781	66.2 ± 11.6
Hx	14,903	10,456/4447	67.0 ± 11.5
PD	17,485	10,841/6644	68.5 ± 10.2
ADP	16,552	10,020/6532	64.9 ± 18.6
AVR	14,827	7914/6913	72.4 ± 10.7
TAR	10,594	7421/3173	69.5 ± 11.6
Descending TAR	5605	4129/1476	69.6 ± 12.3
CABG on-pump	9221	7232/1989	67.7 ± 9.9
CABG off-pump	15,972	12,547/3425	69.1 ± 9.7

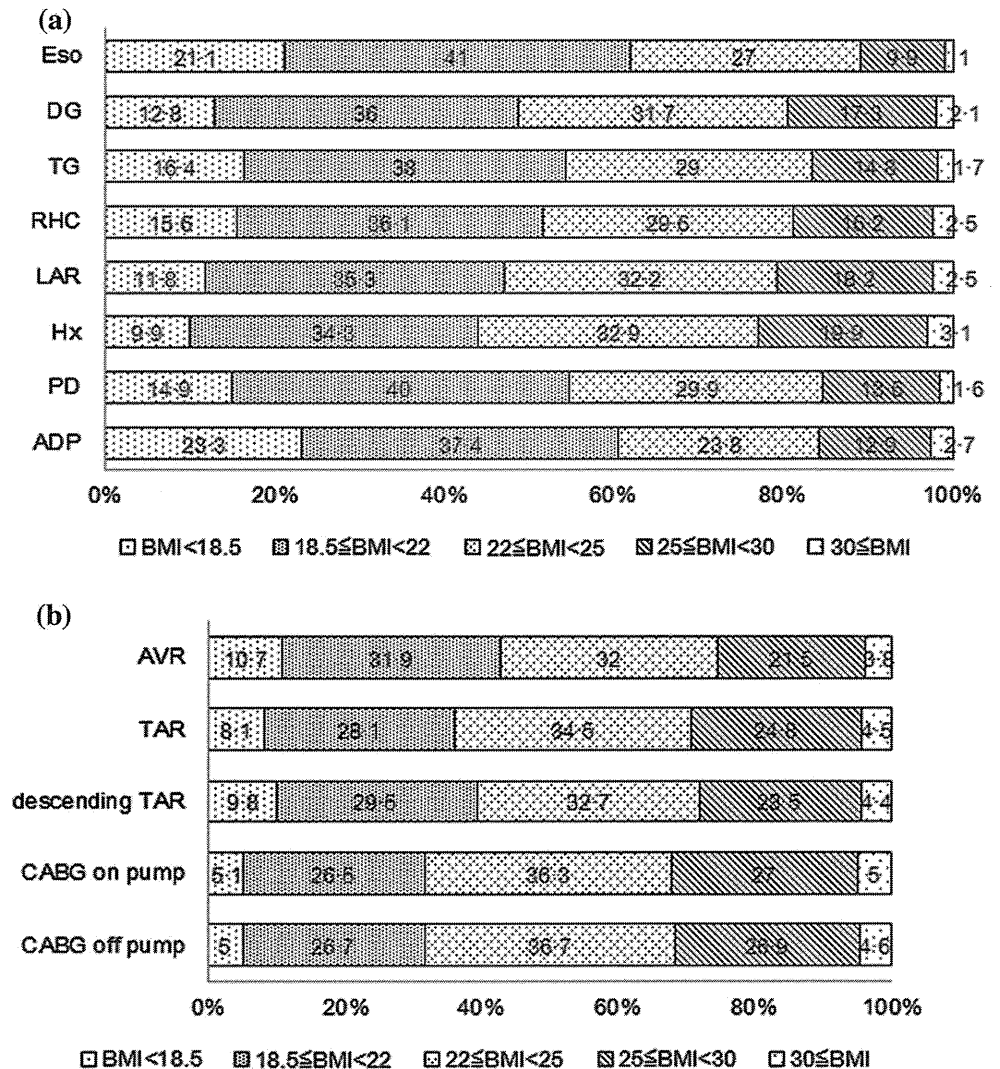
Eso esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment except for the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft

undergoing gastroenterological surgery was less than 20 %, whereas the proportion of overweight patients among those undergoing cardiovascular surgery was more than 20 %. The proportion of obese patients did not exceed 3 % in any of the gastroenterological surgery groups, but it exceeded 4 % in all of the cardiovascular surgery groups, being especially low in the Eso (1 %) group and especially high in the on-pump (5 %) and off-pump (4.6 %) CABG groups. The proportion of underweight patients (with a BMI of <18.5) among those undergoing gastroenterological surgery, apart from Hx, was at least 10 %, whereas among those undergoing cardiovascular surgery, apart from AVR, it was no more than 10 %. This rate was high for ADP (23.3 %), Eso (21.1 %), and PD (14.9 %), but low for off-pump (5 %) and on-pump (5.1 %) CABG.

Operation time by BMI

Figure 2 shows the operation times for all procedures, which became longer as the BMI rose. When a BMI cut-off of 30 was used, the operation time for obese patients was significantly longer than that for those who were not obese, for all procedures except Eso (Table 3). Among the gastroenterological operations, the operation time for obese patients was prolonged for PD (56 ± 8.3 min, mean ± SE), TG (50 ± 4.0 min), and LAR (50 ± 3.9 min), while among the cardiovascular operations, the operation time for obese patients was prolonged for TAR (55 ± 8.4 min) and descending TAR (54 ± 13.8 min). The operation times were originally longer for men than for women, for all of

Fig. 1 a Body mass index (BMI) distribution in the gastroenterological surgery procedures (%). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** BMI distribution in the cardiovascular surgery procedures (%). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft



the procedures (Table 4). The operation time was significantly longer for obese men than for men who were not obese, and this result was consistent among all procedures. The differences in the effects of obesity on operation times between men and women varied among the procedures. The prolongation of operation time by at least 60 min because of obesity was greater in men than in women undergoing LAR, TAR, and descending TAR. Among patients undergoing Hx, the impact of obesity on operation time was greater for women than for men.

Influence of BMI on operative mortality

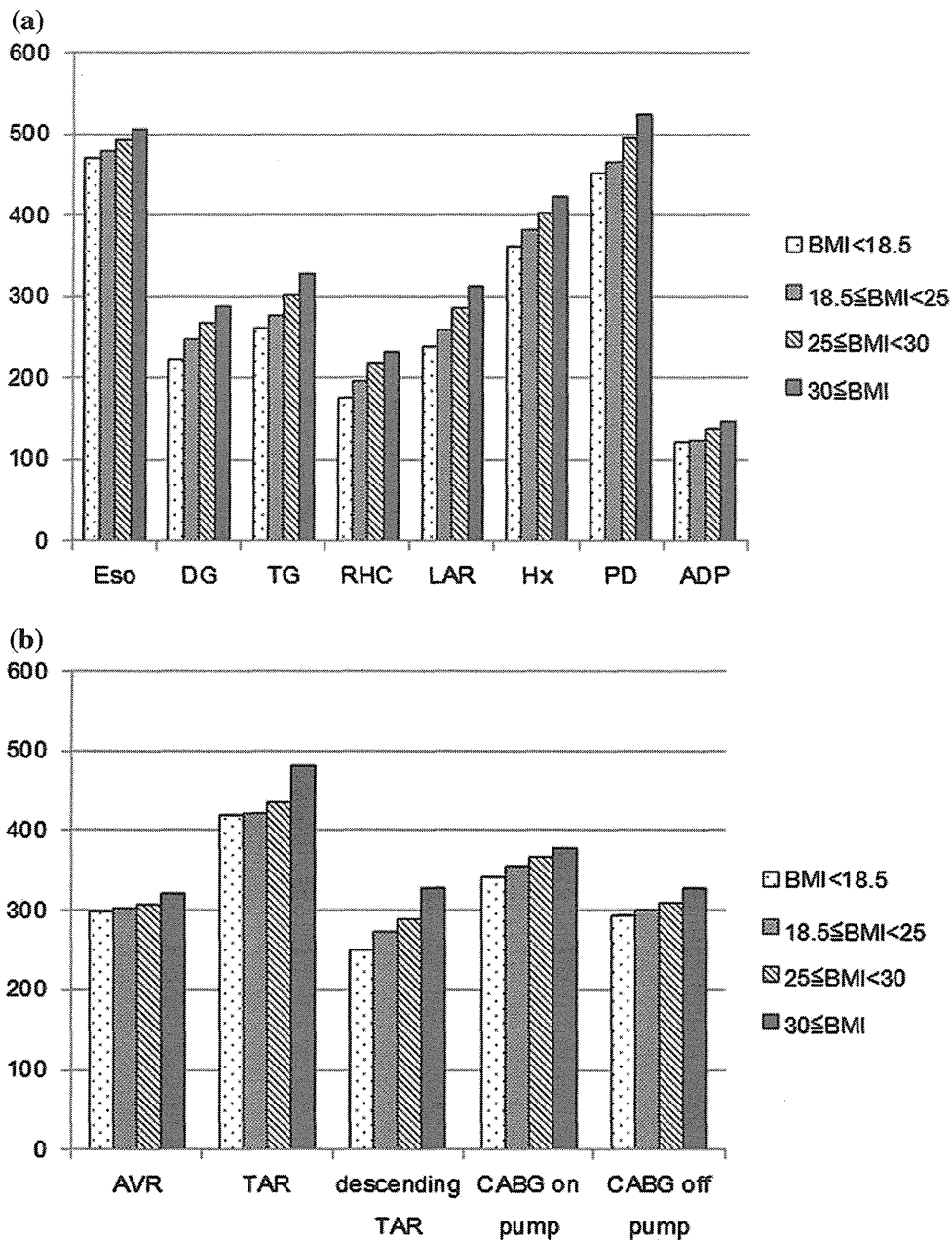
Figure 3 shows the operative mortality rates. The mortality rate according to BMI had a U-shaped distribution for most procedures, with both underweight and obese patients having higher mortality rates. Overweight patients tended

to have the lowest mortality risk among those undergoing cardiovascular surgery, but not among those undergoing gastroenterological surgery. Obesity tended to have a small effect on mortality among patients undergoing Eso or DG. Among patients undergoing PD, those who were underweight had the lowest mortality rate.

Discussion

We conducted a large-scale trans-disciplinary study on the effects of BMI on gastroenterological vs. cardiovascular surgery, using NCD accumulated in Japan. Several previous studies have demonstrated a cause-and-effect relationship between BMI and operative outcomes, including operation time and operative mortality in various fields, including gastroenterological procedures for esophageal

Fig. 2 a Operation times for the gastroenterological surgery procedures (min). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment, apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** Operation times for the cardiovascular surgery procedures (min). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft



cancer [8], gastric cancer [9], colon cancer [10], liver cancer [11], pancreatic cancer [12], and laparoscopic cholecystectomy [13], as well as cardiac procedures, including CABG and valve replacement [14, 15]. However, according to the literature, the influences of BMI on surgery vary among operative procedures and even for the same procedure, so the effects of BMI on operative outcomes remain controversial. To date, two studies involving a large number of cases have been reported. In a study of 30,765 patients undergoing surgery for gastric cancer or colorectal cancer in Japan, Yasanuga et al. found that obese patients had significantly higher rates of postoperative complications and that underweight patients had significantly higher rates of

both postoperative complications and operative mortality than those with a normal BMI [19]. In a study of 13,115 patients undergoing CABG, Alam et al. found that obese patients had significantly prolonged total circulatory bypass and aortic clamp times, as well as an increased risk of postoperative respiratory failure, postoperative renal failure, and surgical site infections, but not of operative mortality [14]. The number of patients in the present study was greater than that in either of the previous studies and we also examined data for various procedures in two major fields. We confirmed that BMI has similar effects on nearly all procedures in the fields of gastroenterological and cardiovascular surgery in this nationwide survey.

Table 3 Operation times (min) according to a body mass index cut-off value of 30

Operation	Total number (BMI < 30:30 ≤ BMI)	Operation time (min)		Prolongation (min)	P value
		BMI < 30	30 ≤ BMI		
Eso	10,825 (10,727:98)	479	505	26	ns
DG	63,650 (62,391:1259)	248	288	40	<0.001
TG	37,817 (37,215:602)	279	329	50	<0.001
RHC	37,750 (36,850:900)	197	233	36	<0.001
LAR	33,217 (32,409:808)	262	312	50	<0.001
Hx	14,903 (14,459:444)	384	424	40	<0.001
PD	17,485 (17,229:256)	468	524	56	<0.001
ADP	16,552 (16,117:435)	127	148	21	<0.001
AVR	14,827 (14,257:570)	304	321	17	<0.001
TAR	10,594 (10,114:480)	426	481	55	<0.001
Descending TAR	5605 (5356:249)	274	328	54	<0.001
CABG on-pump	9221 (8760:461)	358	379	21	<0.001
CABG off-pump	15,972 (15,238:734)	303	328	25	<0.001

Student's *t* test was used to compare the mean operation time between obese (BMI ≥ 30) and non-obese (BMI < 30) patients. Statistical significance was set at *P* < 0.05

Eso esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft, *BMI* body mass index

Operation times were longer for patients with a higher BMI. When a BMI cut-off of 30 was used, the operation time was significantly longer for obese patients for all procedures except Eso. The procedure associated with the greatest prolongation of operation time was PD, by 56 min, while AVR was prolonged by at least 17 min. The results of the previous studies were conflicting about the influences of obesity on operation time, but those of the present study allowed us to conclude that obesity prolongs the operation time for nearly all the procedures studied. Interestingly, for all procedures, the operation times were longer for men than for women, and they were significantly longer for men who were obese than men who were not. We also noted differences among procedures in the prolongation of operation time due to obesity between men and women. It is noteworthy that men typically have a body type characterized by visceral fat accumulation, whereas women tend to show subcutaneous fat accumulation. These body type differences may account for the differences in operative times and the prolongation of surgery because of obesity.

The mortality rates according to BMI showed a U-shaped distribution, with both underweight and obese patients having high mortality rates, except when PD was the procedure performed. Prior reports from Western countries showed similar mortality curves. These studies demonstrated the so-called 'obesity paradox' in that obesity exerts an advantageous effect on morbidity and mortality, compared with normal BMI, in surgical patients [20–22].

Davenport et al. [22] reported that patients with mild obesity, defined as a BMI over 30 but under 35, had a lower 30-day mortality rate than patients of normal weight following vascular surgery. The BMI category with the lowest mortality risk is lower in Asians than in Western populations because Asians have a higher percentage of body fat than Westerners at the same BMI [3, 23]. Deurenberg et al. [24] reported the BMI values of East Asians to be lower, by 1.9–3.2 %, than in Western people when the percentage of body fat was the same. The adverse effect of obesity on short-term prognosis in patients undergoing surgery for a malignant disease would be due to not only the high technical difficulty of the necessary surgical procedures in the obese patient, but to BMI-dependent differences in the severity of the cancer. However, the influence of BMI on malignancy remains controversial [25, 26]. Mullen et al. [27] reported that underweight patients had a significantly higher postoperative death rate, with an odds ratio (OR) of 5.24 and a 95 % confidence interval (CI) of 1.7–16.2, after major surgery for gastrointestinal cancer. As in previous studies, the underweight patients in the present series had higher mortality, which we speculate is related to a reduced capacity to tolerate surgery because of their underlying nutritional deficiencies and probable advanced stages of gastroenterological cancer.

This study has the advantages of being nationwide and including a very large number of cases; however, there are limitations because of its retrospective nature and cross-sectional design. Moreover, certain details were not

Table 4 Operation times (min) according to a body mass index cut-off value of 30 and gender

Operation	Gender	Total number (BMI < 30:30 ≤ BMI)	Operation time (min)		Prolongation (min)	P value
			BMI < 30	30 ≤ BMI		
Eso	Male	9124 (9036:88)	488	521	33	<0.05
	Female	1701 (1691:10)	432	363	−69	ns
DG	Male	42438 (41674:764)	255	303	48	<0.001
	Female	21212 (20717:495)	234	265	31	<0.001
TG	Male	27877 (27484:393)	284	338	54	<0.001
	Female	9940 (9731:209)	264	313	49	<0.001
RHC	Male	18878 (18505:373)	206	251	45	<0.001
	Female	18872 (18345:527)	187	221	34	<0.001
LAR	Male	21,436 (21,013:423)	269	334	65	<0.001
	Female	11,781 (11,396:385)	248	287	39	<0.001
Hx	Male	10,456 (10,162:294)	392	428	36	<0.001
	Female	4447 (4297:150)	368	417	49	<0.001
PD	Male	10,841 (10,715:126)	480	540	60	<0.001
	Female	6644 (6514:130)	448	508	60	<0.001
ADP	Male	10,020 (9790:230)	127	153	26	<0.001
	Female	6532 (6327:205)	126	142	16	<0.001
AVR	Male	7914 (7687:227)	314	354	40	<0.001
	Female	6913 (6570:343)	292	300	8	ns
TAR	Male	7421 (7075:346)	427	494	67	<0.001
	Female	3173 (3039:134)	422	450	28	<0.05
Descending TAR	Male	4129 (3945:184)	275	343	68	<0.001
	Female	1476 (1411:65)	269	286	17	ns
CABG on-pump	Male	7232 (6885:347)	360	380	20	<0.001
	Female	1989 (1875:114)	351	375	24	<0.05
CABG off-pump	Male	12,547 (12,020:527)	305	334	29	<0.001
	Female	3425 (3218:207)	293	312	19	<0.01

Student's *t* test was used to compare the mean operation time between obese (BMI ≥ 30) and non-obese (BMI < 30) patients by sex. Statistical significance was set at $P < 0.05$

Eso esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft, *BMI* body mass index

assessed, such as the presence or absence of endoscopic surgery, emergency vs. non-urgent status, and co-existent illnesses, including hypertension and diabetes. Various factors other than BMI can affect operative outcomes, and these factors differ among operative procedures. It is important to analyze precise risks, including all relevant factors, for a broader range of operative procedures in the future. However, we should consider both obesity and very low body weight as the key factors impacting outcomes.

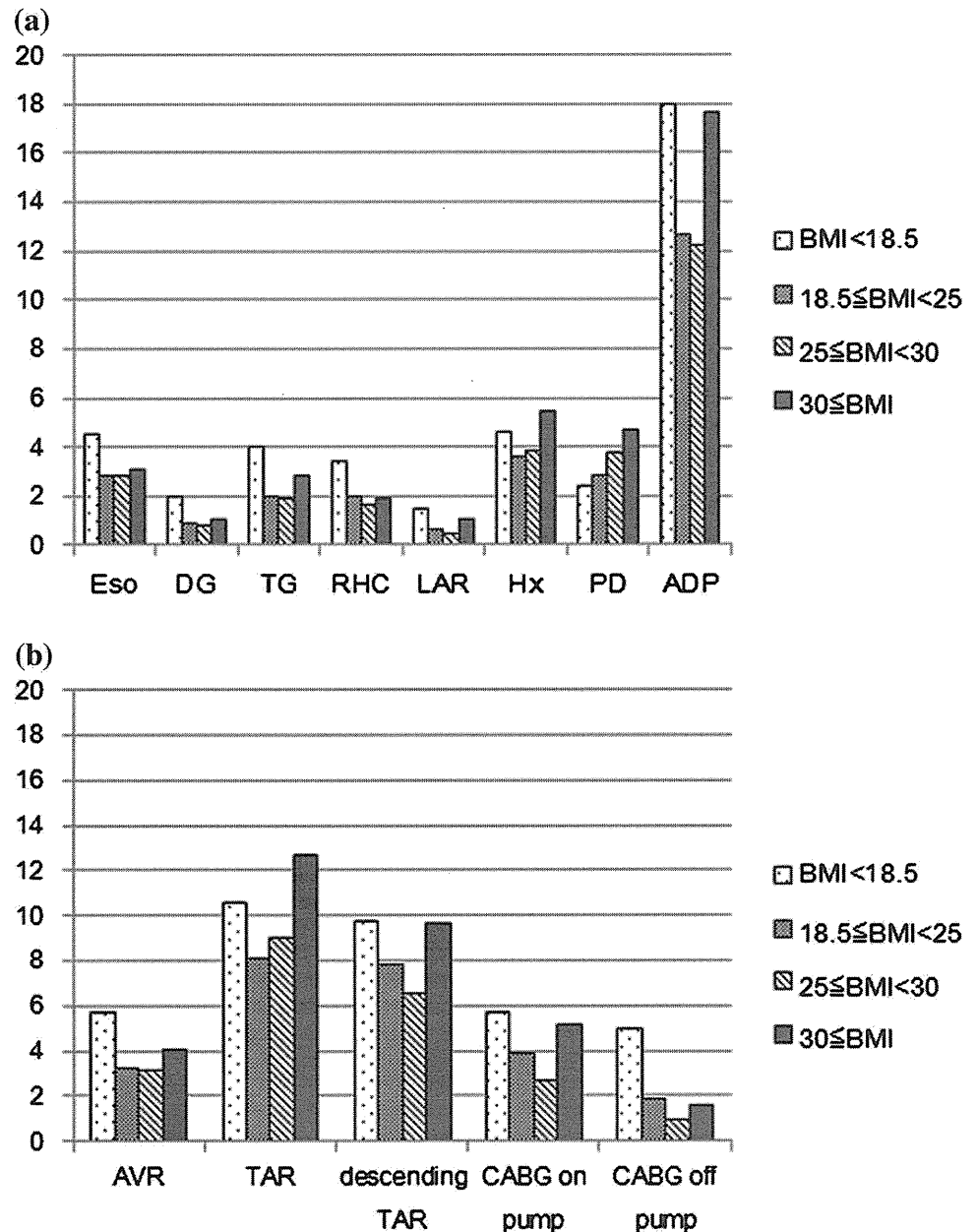
In the present study, a high BMI was shown to influence health economics and inflict excess burden on surgeons, considering the prolonged operation times for all surgical procedures evaluated. Yet, there are no additional fees in relation to obesity, in either Japan or, to our knowledge,

any other country. Given the added burden associated with this condition, it is anticipated that the medical economics of providing surgical treatment for obese patients will be reviewed.

Conclusion

We investigated the effects of BMI on both gastroenterological and cardiovascular surgical procedures based on data from 288,418 patients, obtained from a Japanese nationwide database. The operation time was significantly longer for patients who were obese than for those who were not, for all procedures except *Eso*. Furthermore, both

Fig. 3 a Operative mortality for the gastroenterological surgery procedures (%). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment except for the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** Operative mortality for the cardiovascular surgery procedures (%). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft



obese and underweight patients had high mortality rates. This Japanese nationwide study provides further evidence that obesity and very low bodyweight are both factors with significant adverse effects on operative outcomes.

Compliance with ethical standards

Conflict of interest None of the authors has any conflicts of interest to disclose.

Funding/support This study was funded by the Japan Surgical Society.

Role of the funders/sponsors The NCD data used in this study were collected by the Japan Surgical Society. The Japan Surgical Society reviewed and approved this article before its submission.

References

1. Krishnamurthi RV, Feigin VL, Forouzanfar MH, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of first-ever ischaemic and haemorrhagic stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet Glob Health*. 2013. doi:10.1016/S2214-4109X(13)70089-5.
2. World Health Organization. Global status report on noncommunicable disease 2010. http://www.who.int/nmh/publications/ncd_report_full_en.pdf. Accessed 1 Oct 2014).
3. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;311:806–14.
4. Funatogawa I, Funatogawa T, Nakao M, Karita K, Yano E. Changes in body mass index by birth cohort in Japanese adults:

- results from the National Nutrition Survey of Japan 1956–2005. *Int J Epidemiol.* 2009;38:83–92.
5. Matsushita Y, Takahashi Y, Mizoue T, Inoue M, Noda M, Tsugane S. Overweight and obesity trends among Japanese adults: a 10-year follow-up of the JPHC Study. *Int J Obes (Lond).* 2008;32:1861–7.
 6. Yoshiike N, Seino F, Tajima S, Arai Y, Kawano M, Furuhashi T, et al. Twenty-year changes in the prevalence of overweight in Japanese adults: the National Nutrition Survey 1976–95. *Obes Rev.* 2002;3:183–90.
 7. Kouda K, Nakamura H, Nishio N, Fujita Y, Takeuchi H, Iki M. Trends in body mass index, blood pressure, and serum lipids in Japanese children: Iwata population-based annual screening (1993–2008). *J Epidemiol.* 2010;20:212–8.
 8. Bhayani NH, Gupta A, Dunst CM, Kurian AA, Halpin VJ, Swanson LL. Does morbid obesity worsen outcomes after esophagectomy? *Ann Thorac Surg.* 2013;95:1756–61.
 9. Sugimoto M, Kinoshita T, Shibasaki H, Kato Y, Gotohda N, Takahashi S, et al. Short-term outcome of total laparoscopic distal gastrectomy for overweight and obese patients with gastric cancer. *Surg Endosc.* 2013;27:4291–6.
 10. Makino T, Trencheva K, Shukla PJ, Rubino F, Zhuo C, Pavoors RS, et al. The influence of obesity on short- and long-term outcomes after laparoscopic surgery for colon cancer: a case-matched study of 152 patients. *Surgery.* 2014;156:661–8.
 11. Saunders JK, Rosman AS, Neihaus D, Gouge TH, Melis M. Safety of hepatic resections in obese veterans. *Arch Surg.* 2012;147:331–7.
 12. El Nakeeb A, Hamed H, Shehta A, Askr W, El Dosoky M, Said R, et al. Impact of obesity on surgical outcomes post-pancreaticoduodenectomy: a case-control study. *Int J Surg.* 2014;12:488–93.
 13. Zdichavsky M, Bashin YA, Blumenstock G, Zieker D, Meile T, Konigsrainer A. Impact of risk factors for prolonged operative time in laparoscopic cholecystectomy. *Eur J Gastroenterol Hepatol.* 2012;24:1033–8.
 14. Alam M, Siddiqui S, Lee VV, Elayda MA, Nambi V, Yang EY, et al. Isolated coronary artery bypass grafting in obese individuals: a propensity matched analysis of outcomes. *Circ J.* 2011;75:1378–85.
 15. Smith RL 2nd, Herbert MA, Dewey TM, Brinkman WT, Prince SL, Ryan WH, et al. Does body mass index affect outcomes for aortic valve replacement surgery for aortic stenosis? *Ann Thorac Surg.* 2012;93:742–6.
 16. Watanabe M, Miyata H, Gotoh M, Baba H, Kimura W, Tomita N, et al. Total gastrectomy risk model: data from 20,011 Japanese patients in a Nationwide Internet-Based Database. *Ann Surg.* 2014;260:1034–9.
 17. Kimura W, Miyata H, Gotoh M, Hirai I, Kenjo A, Kitagawa Y, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. *Ann Surg.* 2014;259:773–80.
 18. Dohi M, Miyata H, Doi K, Okawa K, Motomura N, Takamoto S, et al. The off-pump technique in redo coronary artery bypass grafting reduces mortality and major morbidities: propensity score analysis of data from the Japan Cardiovascular Surgery Database. *Eur J Cardiothorac Surg.* 2015;47:299–308.
 19. Yasunaga H, Horiguchi H, Matsuda S, Fushimi K, Hashimoto H, Ayanian JZ. Body mass index and outcomes following gastrointestinal cancer surgery in Japan. *Br J Surg.* 2013;100:1335–43.
 20. Valentijn TM, Galal W, Tjeertes EK, Hoeks SE, Verhagen HJ, Stolker RJ. The obesity paradox in the surgical population. *Surgeon.* 2013;11:169–76.
 21. Mullen JT, Moorman DW, Davenport DL. The obesity paradox: body mass index and outcomes in patients undergoing nonbariatric general surgery. *Ann Surg.* 2009;250:166–72.
 22. Davenport DL, Xenos ES, Hosokawa P, Radford J, Henderson WG, Endean ED. The influence of body mass index obesity status on vascular surgery 30-day morbidity and mortality. *J Vasc Surg.* 2009;49:140–7.
 23. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004;363:157–63.
 24. Deurenberg P, Yap M, van Staveren WA. Body mass index and percent body fat: a meta analysis among different ethnic groups. *Int J Obes Relat Metab Disord.* 1998;22:1164–71.
 25. Seishima R, Okabayashi K, Hasegawa H, Sugiyama D, Ishii Y, Tsuruta M, et al. Obesity was associated with a decreased post-operative recurrence of rectal cancer in a Japanese population. *Surg Today.* 2014;44:2324–31.
 26. Kim SH, Park HS, Kim KH, Yoo H, Chae BJ, Bae JS, et al. Correlation between obesity and clinicopathological factors in patients with papillary thyroid cancer. *Surg Today.* 2015;45:723–9.
 27. Mullen JT, Davenport DL, Hutter MM, Hosokawa PW, Henderson WG, Khuri SF, et al. Impact of body mass index on perioperative outcomes in patients undergoing major intra-abdominal cancer surgery. *Ann Surg Oncol.* 2008;15:2164–72.

Surgical risk model for acute diffuse peritonitis based on a Japanese nationwide database: an initial report on the surgical and 30-day mortality

Tohru Nakagoe · Hiroaki Miyata · Mitsukazu Gotoh · Takayuki Anazawa ·
Hideo Baba · Wataru Kimura · Naohiro Tomita · Mitsuo Shimada ·
Yuko Kitagawa · Kenichi Sugihara · Masaki Mori

Received: 4 March 2014 / Accepted: 12 August 2014 / Published online: 18 September 2014
© Springer Japan 2014

Abstract

Purpose Acute diffuse peritonitis (ADP) is an important surgical complication associated with high morbidity and mortality; however, the risk factors associated with a poor outcome have remained controversial. This study aimed in collecting integrated data using a web-based national database system to build a risk model for mortality after surgery for ADP.

Methods We included cases registered in the National Clinical Database in Japan. After data cleanup, 8,482 surgical cases of ADP from 1,285 hospitals treated between January 1 and December 31, 2011 were analyzed.

Results The raw 30-day and surgical mortality rates were 9.0 and 14.1 %, respectively. The odds ratios (>2.0) for 30-day mortality were as follows: American Society of Anesthesiologists (ASA) class 3, 2.69; ASA class 4, 4.28; ASA class 5, 8.65; previous percutaneous coronary intervention (PCI), 2.05; previous surgery for peripheral vascular disease (PVD), 2.45 and disseminated cancer, 2.16. The odds ratios (>2.0) for surgical mortality were as follows:

ASA class 3, 2.27; ASA class 4, 4.67; ASA class 5, 6.54, and disseminated cancer, 2.09. The C-indices of 30-day and surgical mortality were 0.851 and 0.852, respectively.

Conclusion This is the first report of risk stratification after surgery for ADP using a nationwide surgical database. This system could be useful to predict the outcome of surgery for ADP and for evaluations and benchmark performance studies.

Keywords Acute diffuse peritonitis · Risk factor · Mortality · Risk model

Introduction

Acute diffuse peritonitis (ADP) is an important surgical complication associated with a high incidence of morbidity and mortality [1–4], and is defined as the uncontained rapid spread of an intra-abdominal infection beyond the organ of origin to multiple (2–4) quadrants of the intra-abdominal cavity, regardless of the underlying disease processes, such as a ruptured appendix, ischemic colitis, gastrointestinal (GI) tract perforation, etc. [2–5]. Emergency surgery is defined as a surgery performed on a patient immediately after the diagnosis [6]. Although a definite preoperative diagnosis of a detailed etiology is difficult even using the recently developed imaging modalities [7, 8], the surgical management of ADP involves immediate evacuation of all purulent collections and source control [1–3].

Although the mortality rate from intra-abdominal infections was close to 90 % in the early 1900s, prior to the introduction of the basic principles of surgery, in the modern era, the reduction in mortality to below 20 % has resulted due to the better understanding of the role of damage control, prevention of intra-abdominal compartment

T. Nakagoe · H. Miyata · M. Gotoh · H. Baba · W. Kimura ·
N. Tomita · M. Shimada · Y. Kitagawa
The Japanese Society of Gastroenterological Surgery, Database
Committee, Tokyo, Japan

H. Miyata · M. Gotoh
National Clinical Database (NCD), Tokyo, Japan

M. Gotoh (✉)
Department of Regenerative Surgery, Fukushima Medical
University, 1 Hikarigaoka, Fukushima 960-1295, Japan
e-mail: mgotoh@fmu.ac.jp

T. Anazawa · K. Sugihara · M. Mori
The Japanese Society of Gastroenterological Surgery, Tokyo,
Japan