Further, in regard to the perioperative outcomes between the well-matched groups, the LLR patients had less blood loss, shorter hospital stay, and less morbidity than the OLR patients as shown in Table 3. These results are consistent with the recommendations in the 2nd International Consensus Conference on LLR held in Morioka, Japan, from 4 to 6 October 2014 [28]. However, in the subgroup analysis, major LLR failed to show less blood loss, although it still had shorter hospital stay and less morbidity (Table S1). These significances cannot be blindly accepted as the patient number of each matched group was small. It is also likely that major LLR was in an introduction phase and the learning curve must have an impact during our study period.

With respect to the contents of the complications, the frequency of the liver failure after LLR was lower than after OLR. This result might be explained by less destruction of the collateral blood/lymphatic flow by LLR during mobilization of the liver. Reduction of surgery-induced injury with LLR may lower the risk of liver failure after LLR for HCC patients with severe cirrhosis [29, 30].

In conclusion, compared with OLR, LLR in selected patients with HCC showed similar long-term outcomes, associated with less blood loss, shorter hospital stay, and fewer postoperative complications. Especially, the minor LLR in selected patients is confirmed to be one good option as a standard practice for the treatment of HCC.

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Conflict of interest None declared.

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References

1. Wakabayashi G. Laparoscopic liver resection: how far can we go? J Hepatobiliary Pancreat Surg. 2009;16:403–4.
2. Buell JF, Cherqui D, Geller DA, O'Rourke N, Lannitti D, Dagher I, et al. The international position on laparoscopic liver surgery: the Louisville statement, 2008. Ann Surg. 2009;250:825–30.
3. Nguyen KT, Gamblin TC, Geller DA. World review of laparoscopic liver resection – 2,804 patients. Ann Surg. 2009;250:831–41.
4. 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.
5. Imura S, Shimada M, Utsunomiya T, Morine Y, Wakabayashi G, Kaneko H. Current status of laparoscopic liver surgery in Japan: results of a multicenter Japanese experience. Surg Today. 2014;44: 1214–19.
6. Farges O, Goutte N, Dokmak S, Bendersky N, Falissard B. ACHBT French Hepatectomy Study Group. How surgical technology translates into practice: the model of laparoscopic liver resections performed in France. Ann Surg. 2014;260:916–22.

7. 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.
8. Rubin DB. Estimating causal effects from large data sets using propensity scores. Ann Intern Med. 1997;127(8 Pt 2):757–63.
9. 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.
10. Belli G, Limongelli P, Fantini C, D'Agostino A, Cioffi L, Belli A, et al. Laparoscopic and open treatment of hepatocellular carcinoma in patients with cirrhosis. Br J Surg. 2009;96:1041–8.
11. Tranchart H, Di Giuro G, Lainas P, Roudie J, Agostini H, Franco D, et al. Laparoscopic resection for hepatocellular carcinoma: a matched-pair comparative study. Surg Endosc. 2010;24:1170–6.
12. Sarpel U, Hefti MM, Wisnievsky JP, Roayaie S, Schwartz ME, Labow DM. Outcome for patients treated with laparoscopic versus open resection of hepatocellular carcinoma: case-matched analysis. Ann Surg Oncol. 2009;16:1572–7.
13. Lai EC, Tang CN, Ha JP, Li MK. Laparoscopic liver resection for hepatocellular carcinoma: ten-year experience in a single center. Arch Surg. 2009;144:143–7; discussion 148.
14. Endo Y, Ohta M, Sasaki A, Kai S, Eguchi H, Iwaki K, et al. A comparative study of the long-term outcomes after laparoscopy-assisted and open left lateral hepatectomy for hepatocellular carcinoma. Surg Laparosc Endosc Percutan Tech. 2009;19:e171–4.
15. Kaneko H, Takagi S, Otsuka Y, Tsuchiya M, Tamura A, Katagiri T, et al. Laparoscopic liver resection of hepatocellular carcinoma. Am J Surg. 2005;189:190–4.
16. Cherqui D, Laurent A, Tayar C, Chang S, Van Nhieu JT, Loriau J, et al. Laparoscopic liver resection for peripheral hepatocellular carcinoma in patients with chronic liver disease: midterm results and perspectives. Ann Surg. 2006;243:499–506.
17. Morise Z, Ciria R, Cherqui D, Chen KH, Belli G, Wakabayashi G. Can we expand the indications for laparoscopic liver resection? A systematic review and meta-analysis of laparoscopic liver resection for patients with hepatocellular carcinoma and chronic liver disease. J Hepatobiliary Pancreat Sci. 2015;22:342–52.
18. Nanashima A, Sumida Y, Abo T, Shindou H, Fukuoka H, Takeshita H, et al. Modified Japan integrated staging is currently the best available staging system for hepatocellular carcinoma patients who have undergone hepatectomy. J Gastroenterol. 2006;41:250–6.
19. Ikai I, Takayasu K, Omata M, Okita K, Nakanuma Y, Matsuyama Y, et al. A modified Japan integrated stage score for prognostic assessment in patients with hepatocellular carcinoma. J Gastroenterol. 2006;41:884–92.
20. 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;22:2344–9.
21. Strasberg SM. Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. J Hepatobiliary Pancreat Surg. 2005;12:351–5.
22. Matsumoto K, Yoshimoto J, Sugo H, Kojima K, Futagawa S, Matsumoto T. Relationship between the histological degrees of hepatitis and the postoperative recurrence of hepatocellular carcinoma in patients with hepatitis C. Hepatol Res. 2002;23:196–201.
23. Mirnezami R, Mirnezami AH, Chandrakumaran K, Abu Hilal M, Pearce NW, Primrose JN, et al. Short- and long-term outcomes after laparoscopic and open hepatic resection: systematic review and meta-analysis. HPB (Oxford). 2011;13:295–308.
24. 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.
25. Li N, Wu YR, Wu B, Lu MQ. Surgical and oncologic outcomes following laparoscopic versus open liver resection for hepatocellular carcinoma: a meta-analysis. Hepatol Res. 2012;42:51–9.
26. Kim H, Suh KS, Lee KW, Yi NJ, Hong G, Suh SW, et al. Long-term outcome of laparoscopic versus open liver resection for hepatocellular carcinoma: a case-controlled study with propensity score matching. Surg Endosc. 2014;28:950–60.
27. 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.
28. Wakabayashi G, Cherqui D, Geller DA, Buell JF, Kaneko H, Han HS, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg. 2015;261:619–29.
29. Kanazawa A, Tsukamoto T, Shimizu S, Kodai S, Yamazoe S, Yamamoto S, et al. Impact of laparoscopic liver resection for hepatocellular carcinoma with F4-liver cirrhosis. Surg Endosc. 2013;27:2592–7.
30. Morise Z, Kawabe N, Tomishige H, Nagata H, Kawase J, Arakawa S, et al. Recent advances in the surgical treatment of hepatocellular carcinoma. World J Gastroenterol. 2014;20:14381–92.

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 perioperative outcomes according to the surgical procedure.
Fig. S1 Receiver operating characteristics (ROC) curve.
Fig. S2 Histogram of propensity score before and after PSM.
Fig. S3 Standardized differences before and after PSM.

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ORIGINAL ARTICLE

Long-term and perioperative outcomes of laparoscopic versus open liver resection for colorectal liver metastases with propensity score matching: a multi-institutional Japanese study

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Abstract

Background The aim of the present study was to clarify the surgical outcome and long-term prognosis of laparoscopic liver resection (LLR) compared with conventional open liver resection (OLR) in patients with colorectal liver metastases (CRLM).
Methods A one-to-two propensity score matching (PSM) analysis was applied. Covariates ($P < 0.2$) used for PSM estimation included preoperative levels of CEA and CA19-9; primary tumor differentiation; primary pathological lymph node metastasis; number, size, location, and distribution of CRLM; existence of extrahepatic metastasis; extent of hepatic resection; total bilirubin and prothrombin activity levels; and preoperative chemotherapy. Perioperative data and long-term survival were compared.
Results From 2005 to 2010, 1,331 patients with hepatic resection for CRLM were enrolled. By PSM, 171 LLR and 342 OLR patients showed similar preoperative clinical characteristics. Median estimated blood loss (163 g vs 415 g, $P < 0.001$) and median postoperative hospital stay (12 days vs 14 days; $P < 0.001$) were significantly reduced in the LLR group. Morbidity and mortality were similar. Five-year rates of recurrence-free, overall, and disease-specific survival did not differ significantly. The R0 resection rate was similar.
Conclusions In selected CRLM patients, LLR is strongly associated with lower blood loss and shorter hospital stay and has equivalent long-term survival comparable with OLR.

Keywords Colorectal liver metastases · Laparoscopic liver resection · Open liver resection · Propensity score matched analysis

Introduction

Hepatic resection is a highly curative treatment for colorectal liver metastases (CRLM) usually providing excellent long-term survival, with 5- and 10-year overall survival (OS) rates being 33%–58% and 23%–39%, respectively [1–5]. Recent data demonstrated the superiority of hepatic resection to thermal ablation for CRLM [6, 7]. Advances in chemotherapy and targeted therapy may render initially unresectable CRLM patients eligible for hepatic resection and may improve prognosis, particularly in those patients who respond to induction therapy [8, 9]. CRLM may often recur even after curative resection, and repeated hepatectomy is obviously useful for such patients [10, 11]. Based on a worldwide survey, the long-term survival after the first to the fourth hepatic resection for patients with CRLM is almost similar [11].

Laparoscopic liver resection (LLR) was initially applied only to limited resections, including partial resection or left lateral sectionectomy. The pure laparoscopic approach (Pure), the hand-assisted laparoscopic approach (HALS), and the hybrid technique (Hybrid) were defined in the 2008 1st International Consensus Conference on Laparoscopic Liver Resection (ICCLLR) in Louisville, KY, USA [12]. These approaches are typically selected based on individual tumor size and location, background liver factors, and individual preference of the surgical team. Nowadays, the indication of LLR for CRLM has expanded from metastases located in anterolateral positions to those located in posterosuperior positions [13]. Hemihepatectomy or anatomic resection of the segment and sector can also be used for CRLM patients according to the 2014 2nd ICCLLR in Morioka, Iwate, Japan [14].

Several studies have demonstrated that LLR is associated with better short-term outcomes, including reduced intraoperative bleeding, a lower morbidity rate, and a shorter hospital stay compared with conventional open liver resection (OLR) [15–18]. Additional advantages include reduction of tissue damage, surgical stress, and overall costs [19, 20]. Several articles have focused on the better oncological and surgical results enabled by LLR [21–30]. However, most of these findings were based on retrospective analyses of case-matched studies or meta-analyses of non-randomized studies. Recently, a small-size propensity score matching (PSM) study of CRLM patients reported that LLR results in significantly lower blood loss, lower morbidity, and shorter hospital stay [31–33].

Multiple selection biases exist with regard to allocating patients for LLR. To obtain enough numbers of CRLM patients undergoing hepatectomy for analysis, we conducted a multicenter study involving Japanese specialized centers for both hepatobiliary and endoscopic surgery. In addition, we performed a PSM analysis, which enables comparison between different therapies with reduced selection bias in retrospective studies [34–36]. Recently, it was reported that there is no statistically significant difference with regard to treatment effect between non-randomized studies involving suitable PSM analysis and randomized controlled trials (RCT) [37]. This study was undertaken to determine the surgical outcome and long-term prognosis of LLR in comparison with those of conventional OLR for CRLM patients.

Methods

This clinical study was performed by the "Project Committee of the Endoscopic Surgery" of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. From January 2005 to December 2010, practically all patients with CRLM treated with initial hepatic resection were enrolled. Patients had a histologically proven diagnosis of colorectal cancer with synchronous or metachronous liver metastases. Perioperative chemotherapy was performed based on the policy of each individual institution. Hepatic resection modality was recorded in accordance with the terms established by the International Hepato-Pancreato-Biliary Association, Brisbane, Australia, 2000 [38]. Liver resection of three segments or more was defined as major liver resection. Difficult tumor location was defined as tumors situated in the posterosuperior segments of the liver (segments 1, 7, and 8) [13]. Gender (female, male), age (≤70, >70), body mass index (BMI) (≤25, >25), hepatitis B surface antigen (HBs-Ag; negative, positive), hepatitis C antibody (HCV-Ab; negative, positive), American Society of Anesthesiologists (ASA) physical status classification (1–2, ≥3), disease-free interval (DFI) between primary tumor and liver metastases (≤1 year, >1 year), preoperative levels of carcinoembryonic antigen (CEA; ≤100 ng/ml, >100 ng/ml) and carbohydrate antigen 19-9 (CA19-9; ≤100 U/ml, >100 U/ml), primary tumor differentiation (well, moderately, poorly, and mucinous), vessel invasion and lymphatic invasion of the primary tumor (negative, positive), primary pathological lymph node (LN) metastasis (negative, positive), location of primary sites (colon, rectum), timing of liver metastases (synchronous, metachronous), tumor number (1, 2–4, ≥5) [39], tumor size (≤5 cm, >5 cm), tumor location (difficult, non-difficult), tumor distribution (unilobar, bilobar), existence of extrahepatic metastasis (yes, no), hilar lymph node metastasis (yes, no), coexistence of radiofrequency ablation (RFA; yes, no), extent of hepatic resection (major, minor) were investigated prior to surgery. All patients also underwent preoperative liver function tests, including those measuring total bilirubin (≤2 mg/ml, >2 mg/ml) and albumin (≥3.5 g/dl, <3.5 g/dl) levels, prothrombin activity (≥80%, <80%), 15-min indocyanine retention rate (ICG R15; ≤15%, >15%), and Child–Pugh score (A, B). The presence or absence of pre- and postoperative chemotherapy (yes, no) was recorded. All data were collected retrospectively in 2014 using a shared database for CRLM produced by the Japanese Society of Hepato-Biliary-Pancreatic Surgery and the Japanese Society for Cancer of the Colon and Rectum. This study was approved by the institutional review board (IRB) (approval number, 798; Kumamoto University) and the ethics committee of the Japanese Society of Hepato-Biliary-Pancreatic Surgery and conducted in accordance with the mandates of the Helsinki Declaration 2013.

Operative procedure

Selection of LLR vs OLR was based on individual institutional strategies according to tumor size and location, liver function, and the volume of the future remnant liver [40]. Similarly, LLR operative procedures were selected by surgeons depending on their familiarity with and understanding of the instruments and individual procedures [41]. LLR can be performed using a Pure, HALS, or Hybrid approach as defined by the 2008 Consensus Conference [12].

Intraoperative and postoperative parameters

Intraoperative blood loss, operative time, and frequency of red cell concentrate (RCC) administration were recorded. Morbidity was graded according to the Clavien–Dindo classification [42], and adverse events of grade IIIA or more were defined as morbidity.

Surgical site infection (SSI), bile leakage, pleural effusion/ascites, postoperative intra-abdominal bleeding, ileus, and high bilirubinemia were registered. SSI included superficial and deep incisional SSI. Other morbidities were recorded separately. Moreover, 1- and 3-month mortality was evaluated. Final curability (R0, R1, R2) was assessed by histological investigation of resected specimens. Surgical margins were measured at the cutting surfaces of resected specimens. The number of postoperative hospital days was assessed for each patient.

Recurrence and survival

The starting point was the day of initial hepatic resection. Causes of death were recorded as either colorectal cancer-related or related to other causes. All deaths and recurrences of colorectal cancer were estimated for calculation of recurrence-free survival (RFS). OS and disease-specific survival (DSS) were calculated using the overall number of deaths and deaths specifically due to colorectal cancer, respectively. Size, number, and location of the initial recurrent tumor and the time to the first recurrence were recorded. The initial recurrence pattern was characterized as being intrahepatic only, extrahepatic only, or both intra- and extrahepatic. The number of patients who exhibited recurrence at the cutting surface of the liver was recorded.

Statistical analyses

A PSM analysis [34–36] was used to build a matched group of patients for comparison of clinical and survival outcomes between the LLR and OLR groups. In the overall sample, the patients' characteristics listed in Table 1 (30 variables in total) were compared between LLR and OLR using the Fisher's exact test for categorical variables and Wilcoxon rank-sum (Mann–Whitney) test for continuous variables. Possible confounders were chosen for their potential association with the outcome of interest based on clinical knowledge. The PS model was estimated using a logistic regression model that adjusted for the variables that had $P < 0.20$ in Table 1 (13 variables in total) and ensuring that the proportion of missing data was below 25%. Each LLR patient was matched to an OLR patient using 1-to-2 optimal data matching by Mahalanobis Distance within Propensity Score Calipers in random order without replacement [35]. Propensity scores were matched using a caliper width 1.0 logit of the SD to achieve a good covariate balance. The standardized differences were used to measure covariate balance, whereby an absolute standardized difference above 10% represents meaningful imbalance. Of patients who underwent LLR, 81.4% (171 out of 210) were matched to similar patients who underwent OLR. The covariate balance in the matched cohort was considerably improved.

The Kaplan–Meier method was used to calculate 5-year survival rates, the log-rank test for calculating *P*-values for the overall cohort, and the stratified Cox proportional hazard regression model for the matched cohort for RFS, OS, and DSS. Other paired comparisons were performed using conditional logistic regression analysis for categorical variables and Wilcoxon signed rank test for continuous variables [35]. Binomial exact was used to calculate 95% confidence interval for median observation period unless otherwise indicated. A *P*-value of <0.05 was considered statistically significant. Statistical analyses were performed using the Stata Statistical Software: Release 13.1 (StataCorp LP, College Station, TX, USA), and the NCSS 10 Statistical Software (2015) (Kaysville, UT, USA).

Results

A total of 1,331 CRLM patients undergoing laparoscopic or open liver resection were evaluated, and they were divided into two groups: the LLR group ($n = 210$) and the OLR group ($n = 1{,}121$). The proportion of LLR was 15.8%. The ratio of LLR was 6.2% in the first half (2005 to 2007) and 23.1% in the second half (2008 to 2010) of the study. In the overall cohort, LLR involved the Pure (62%), the HALS (9%), and the Hybrid (29%) approaches. Partial hepatectomy, segmentectomy or sectionectomy and hemihepatectomy were selected in 71.1%, 24.2%, and 5.8% in the LLR group and 64.6%, 25.7%, and 9.7% in the OLR group. In overall cohort, univariate analysis revealed the following 13 positively related factors ($P < 0.2$) among the 30 factors: serum levels of CEA and CA19-9; primary tumor differentiation; pathological LN metastasis; number, size, location and distribution of CRLM; extrahepatic metastasis; extent of hepatic resection; total bilirubin and prothrombin activity; and postoperative chemotherapy.

After one-to-two case propensity matching, a total of 171 LLR and 342 OLR patients were subjected to further analysis. Patient characteristics of the overall cohort and PSM cohort are displayed in Table 1. All baseline characteristics in the PSM cohort except timing of liver metastases were comparable between the two groups, and the proportion of synchronous

Table 1 Patients' characteristics underwent laparoscopic liver resection (LLR) and open liver resection (OLR): the overall cohort and propensity score matching (PSM) cohort

	Overall cohort ($n = 1,331$)			PSM cohort ($n = 513$)		
	LLR ($n = 210$)	OLR ($n = 1,121$)	P-value	LLR ($n = 171$)	OLR ($n = 342$)	P-value
Patient factors						
Age (≤70, >70)	142: 68	800: 320	0.282	110: 61	239: 103	0.356
Gender (male, female)	134: 76	721: 395	0.814	107: 64	215: 126	0.816
BMI (≤25, >25)	164: 46	844: 277	0.430	131: 40	261: 81	0.940
HCV-Ab (yes, no)	5: 198	34: 925	0.526	5: 161	8: 323	0.811
HBs-Ag (yes, no)	3: 200	20: 938	0.783	1: 165	6: 324	0.344
ASA (1-2, 3≤)	187: 7	911: 42	0.845	161: 5	288: 10	0.965
DFI (≤1 year, >1 year)	139: 71	784: 337	0.290	119: 52	231: 111	0.536
CEA levels (≤100 ng/ml, >100 ng/ml)	191: 8	776: 95	0.002	165: 6	330: 12	0.968
CA19-9 levels (≤100 IU/ml, >100 IU/ml)	177: 19	697: 152	0.005	157: 14	309: 33	0.865
Total bilirubin (≤2 mg/dl, >2 mg/dl)	205: 5	968: 153	<.001	170: 1	340: 2	>.999
Albumin (≥3.5 g/dl, <3.5 g/dl)	22: 188	111: 1010	0.802	19: 152	22: 320	0.083
Prothrombin activity (≥80%, <80%)	11: 199	108: 1013	0.047	8: 163	14: 328	0.730
ICG R15 (≤15%, >15%)	141: 69	731: 390	0.635	116: 55	256: 86	0.081
Child–Pugh score (A, B)	209: 1	1095: 26	0.107	171: 0	339: 3	-
Pre-operative chemotherapy (yes, no)	38: 172	245: 876	0.234	30: 141	67: 275	0.801
Postoperative chemotherapy (yes, no)	108: 102	633: 488	0.198	87: 84	195: 147	0.638
Primary lesion factors						
Tumor differentiation (well/moderately/poorly and mucinous)	53: 137: 10	315: 585: 50	0.172	42: 120: 9	90: 241: 11	0.719
Vessel invasion (negative, positive)	46: 147	218: 705	0.926	37: 128	89: 242	0.236
Lymphatic invasion (negative, positive)	51: 143	227: 714	0.522	45: 121	96: 237	0.556
Primary pathological lymph node (negative, positive)	81: 109	297: 513	0.135	75: 96	134: 208	0.517
Location of primary sites (colon or rectum)	106: 84	547: 379	0.419	90: 70	173: 142	0.667
Liver metastases factors						
Timing of liver metastases (synchronous, metachronous)	83: 127	474: 647	0.493	69: 102	107: 235	0.015
Tumor number (1, 2-4, ≥5)	149: 52: 2	570: 400: 96	<.001	127: 43: 1	251: 89: 2	0.251
Tumor size (≤5 cm, >5 cm)	202: 6	1018: 82	0.015	167: 4	334: 8	0.924
Tumor location (difficult, non-difficult)	80: 130	645: 470	<.001	68: 103	154: 188	0.968
Tumor distribution (unilobar, bilobar)	174: 36	762: 353	<.001	143: 28	283: 59	0.566
Extrahepatic metastasis (yes, no)	9: 201	89: 1025	0.062	7: 164	13: 329	0.690
Hilar lymph node metastasis (yes, no)	0: 101	11: 720	0.378	0: 78	3: 204	0.992
Coexistence of RFA (yes, no)	5: 205	40: 1081	0.532	5: 166	8: 334	0.445
Extent of hepatic resection (major, minor)	12: 198	103: 1018	0.109	10: 161	20: 322	0.682

ASA American Society of Anesthesiologists, *BMI* body mass index, *CA19-9* carbohydrate antigen 19-9, *CEA* carcinoembryonic antigen, *DFI* disease-free interval, *HBs-Ag* hepatitis B surface antigen, *HCV-Ab* anti-hepatitis C antibody, *ICG R15* indocyanine green retention rate at 15 min, *RFA* radio-frequency ablation

Clinical parameters were compared with Fisher's exact test for overall cohort, and 5-stratified conditional logistic regression for PSM cohort

CRLM was larger in LLR patients. Patients' continuous factors were listed as median value with range (Table S1). In the PSM cohort, LLR was applied for selected CRLM patients with one metastasis (max, 5), 2.2 cm in diameter (max, 8.4 cm) and slightly elevated CEA level of 7.1 ng/ml and normal CA19-9 level of 16.2 IU/ml. Percentage of patients with a difficult tumor location was 39.8%. Our initial study with $P < 0.05$ yielded eight factors, which reduced to five after stepwise logistic regression. We set the cutoff level to $P < 0.20$ with the proceeding logistics without stepwise analyses to cover more factors in clinical aspects. Standardized differences before and after PSM are demonstrated (Fig. S1). Imbalances were defined as an absolute value greater than 10%. The receiver operating characteristic (ROC) curves were used to evaluate the accuracy of PSM. The area under the curve of the propensity score for LLR was 0.693.

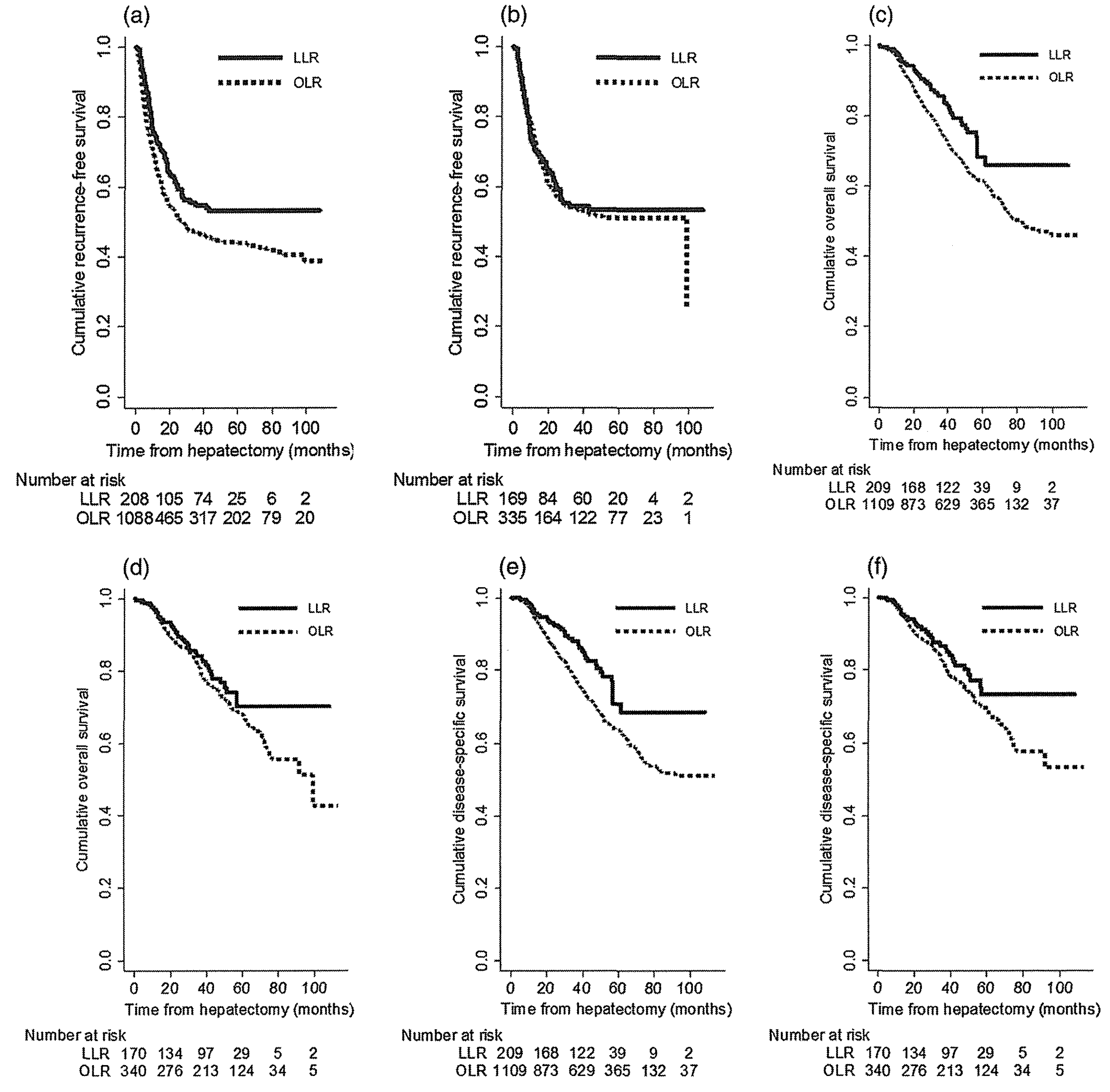

Fig. 1 Kaplan–Meier survival curves comparing recurrence-free survival (RFS), overall survival (OS), and disease-specific survival (DSS) in the overall ($n = 1,331$) and propensity score matching (PSM) cohorts ($n = 513$). (**a**) RFS in the overall cohort; (**b**) RFS in the PSM cohort; (**c**) OS in the overall cohort; (**d**) OS in the PSM cohort; (**e**) DSS in the overall cohort; (**f**) DSS in the PSM cohort. Solid line, laparoscopic liver resection (LLR); dotted line, open liver resection (OLR). Standardized differences before and after PSM. Open circle, before propensity matching; closed triangle, after propensity matching

Intraoperative parameters

In the PSM cohort, the median operative time (282 min vs 277 min, $P = 0.130$) was comparable, and median blood loss (163 g vs 415 g, $P < 0.001$) and the ratio of blood loss larger than 1,000 mL (6.5% vs 16.5%, $P = 0.004$) were significantly lower in the LLR group than in the OLR group (Table 2). The frequency of RCC transfusion did not differ significantly across the two groups (8.4% vs 4.4%, $P = 0.148$). R0, R1, and R2 resection was performed for 92.2%, 5.4%, and 3.0% patients in the LLR group and in 95.5%, 2.4%, and 2.1% in the OLR group. R2 resection included resection with ablation (four patients in the LLR group and six in the OLR group). Curability was similar across the two groups. The median pathological surgical margin was comparable ($P = 0.963$), namely 5 (0–40) mm and 5 (0–45) mm by LLR and OLR, respectively.

Postoperative morbidity and mortality

In the PSM cohort, postoperative complication rates (14.1% vs 12.7%, $P = 0.631$), and the level of morbidity were comparable across the two groups (Table 2). Postoperative complications following LLR in the PSM cohort included incisional SSI (3.5%), bile leakage (2.9%), ascites and pleural effusion (1.2%), and intra-abdominal hemorrhage (0.6%); in addition, leakage of

Table 2 Perioperative outcome of colorectal liver metastases (CRLM) patients who underwent laparoscopic liver resection (LLR) and open liver resection (OLR): the overall cohort and propensity score matching (PSM) cohort

	Overall cohort (n = 1,331)			PSM cohort (n = 513)		
	LLR (n = 210)	OLR (n = 1,121)	P-value	LLR (n = 171)	OLR (n = 342)	P-value
Operation time (min) median (range)	281 (60-1120)	312 (39-3350)	0.020	282 (60-1120)	277 (40-1343)	0.130
Blood loss (g), median (range)	160 (0-3355)	500 (0-11240)	<0.001	163 (0-3355)	405 (0-11240)	<0.001
Blood loss ≥ 1,000 (g) (yes, no)	15: 192	211: 813	<0.001	11: 159	55: 278	0.004
pRBC administration (%)	8.7	16.6	0.004	8.4	12.8	0.148
R0	190	929		154	315	
R1	9	60		9	8	
			0.899			0.120
R2	1	7		1	1	
R0+ablation	4	26		4	6	
Pathological surgical margin (mm), median (range)	5 (0-40)	5 (0-50)	0.203	5 (0-40)	5 (0-45)	0.963
Morbidity (%)	13.0	13.4	>0.999	14.1	12.7	0.631
Mortality (%) within 1 month	0.0	0.1	>0.999	0.0	0.0	N.A.
within 3 months	0.0	0.5	>0.999	0.0	0.6	N.A.
Postoperative hospitalization (days), median (range)	12 (1-192)	16 (2-745)	<0.001	12 (3-192)	14 (4-174)	<0.001

N.A. not applicable, *pRBC* packed red blood cell

Clinical parameters were compared with; Overall cohort: Wilcoxon rank-sum (Mann–Whitney) test for ordinal, and Fisher's exact test for categorical data. PSM cohort: 5-stratified conditional logistic regression for ordinal, and 5-stratified conditional logistic regression for categorical

intestinal anastomosis (3.5%) and organ/space SSI (3.5%) were seen. No patients experienced intestinal bleeding, intestinal obstruction, or hyperbilirubinemia. No patients experienced port site recurrence or dissemination, even in the overall cohort and one patient experienced port site hernia. In the PSM cohort, no fatalities were observed in the LLR group within 3 months, while there were two fatalities within 3 months in the OLR group.

Postoperative hospital stay

Median postoperative hospital stay was significantly shorter for LLR patients than for OLR patients [12 days (range, 3–192 days) vs 14 days (range, 4–174 days), $P < 0.001$; Table 2].

Postoperative survival and recurrence

In the overall cohort, RFS, OS, and DSS curves were significantly superior for LLR patients compared with those for OLR patients (Fig. 1a,c,e): RFS ($P = 0.013$), OS ($P = 0.004$), or DSS ($P = 0.004$). In the propensity-matched cohort, median observation periods were different between the two procedures (LLR, 41.7 months; 95% CI, 39.5–44.2; OLR, 49.1 months; 95% CI, 44.4–52.4). The cumulative 1-, 3-, and 5-year RFS rates were 70.7%, 54.5%, and 53.4%, respectively, for the LLR group and 73.4%, 53.5%, and 51.2%, respectively, for the OLR group (Fig. 1b). The cumulative 1-, 3-, and 5-year OS rates were 96.3%, 84.2%, and 70.1%, respectively, for the LLR group and 96.0%, 80.8%, and 68.0%, respectively, for the OLR group (Fig. 1d). The cumulative 1-, 3-, and 5-year DSS rates were 96.8%, 86.8%, and 73.2%, respectively, for LLR patients and 96.6%, 82.2%, and 69.8%, respectively, for OLR patients (Fig. 1f). No significant differences in RFS ($P = 0.953$), OS ($P = 0.299$), or DSS ($P = 0.218$) were observed between the two groups. Recurrence at the cutting line was encountered in 3.5% by LLR and 3.5% by OLR, and the ratios were considered similar in the two groups ($P = 0.890$). The initial recurrence patterns were assessed, and recurrence classified as "intrahepatic only" was similar (22.0% vs 19.5%, $P = 0.370$), "extrahepatic only" was significantly less commonly observed in the LLR group than in the OLR group (19.0% vs 33.0%, $P = 0.001$), and "intra- and extrahepatic recurrence" was significantly more in the LLR group than in the OLR group (15.7% vs 7.2%, $P = 0.003$). As intrahepatic recurrences, the largest tumor diameters at first recurrence were considered marginally smaller in the LLR group ($P = 0.058$); 17 (1–60) mm in the LLR group and 20 (2–70) mm in the OLR group. The frequency of solitary recurrences was similarly observed (55.9% vs 56.8%; $P = 0.812$). The time elapsed to the first recurrence was comparable ($P = 0.145$); 9.1 (0.9–95.6) months in the LLR group and 12.7 (0.9–110.2) months in the OLR group.

Discussion

A web-based international survey of the global application of LLR was reported prior to the 2nd ICCLLR in Iwate, Japan

[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.

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References

1. 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.
2. 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.
3. 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.
4. Cummings LC, Payes JD, Cooper GS. Survival after hepatic resection in metastatic colorectal cancer: a population-based study. Cancer 2007;109:718–26.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. Rao A, Rao G, Ahmed I. Laparoscopic or open liver resection? Let systematic review decide it. Am J Surg. 2012;204:222–31.
19. 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. Guerron 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.

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ORIGINAL ARTICLE

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

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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 ($n = 2{,}010$)			After PSM ($n = 1{,}458$)		
	ODP (1,108)	LDP (902)	P	ODP (729)	LDP (729)	P
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 ($P < 0.05$).

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.

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 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.

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References

1. Cuschieri A, Jakimowicz JJ, van Spreeuwel J. Laparoscopic distal 70% pancreatectomy and splenectomy for chronic pancreatitis. Ann Surg. 1996;223:280–5.
2. Gagner M, Pomp A, Herrera MF. Early experience with laparoscopic resections of islet cell tumors. Surgery. 1996;120:1051–4.
3. 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.
4. DiNorcia 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.
5. 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.
6. 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.
7. 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.
8. Jusoh AC, Ammori BJ. Laparoscopic versus open distal pancreatectomy: a systematic review of comparative studies. Surg Endosc. 2012;26:904–13.
9. 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.
10. 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.
11. Abu Hilal M, Takhar AS. Laparoscopic left pancreatectomy: current concepts. Pancreatology. 2013;13:443–8.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. 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 Warshaw procedure. Pancreatology. 2014;14:530–5.
22. Yu X, Li H, Jin C, Fu D, Di Y, Hao S, et al. Splenic vessel preservation versus Warshaw's technique during spleen-preserving distal pancreatectomy: a meta-analysis and systematic review. Langenbecks Arch Surg. 2015;400:183–91.
23. 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.
24. 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.
25. 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.

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ORIGINAL ARTICLE

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

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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.

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

Year	References	n	Disease	Operation	BMI cut-off values	Operation time (min) P value	Mortality (%) P 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 $\geq$ 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),