**Propensity score-based analysis of outcomes of laparoscopic *versus* open liver resection for colorectal metastases**

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**Background:**There is a need for high-level evidence regarding the added value of laparoscopic (LLR) compared with open (OLR) liver resection. The aim of this study was to compare the surgical and oncological outcomes of patients with colorectal liver metastases (CRLM) undergoing LLR and OLR using propensity score matching to minimize bias.

**Methods:**This was a single-centre retrospective study using a prospective database of patients undergoing liver resection for CRLM between August 2004 and April 2015. Co-variables selected for matching included: number and size of lesions, tumour location, extent and number of resections, phase of surgical experience, location and lymph node status of primary tumour, perioperative chemotherapy, unilobar or bilobar disease, synchronous or metachronous disease. Prematching and postmatching analyses were compared. Surgical and oncological outcomes were analysed.

**Results:**Some 176 patients undergoing LLR and 191 having OLR were enrolled. After matching, 133 patients from each group were compared. At prematching analysis, patients in the LLR group showed a longer overall survival (OS) and higher R0 rate than those in the OLR group (*P*= 0.047 and *P*= 0.030 respectively). Postmatching analyses failed to confirm these results, showing similar OS and R0 rate between the LLR and OLR group (median OS: 55.2 *versus* 65.3 months respectively, hazard ratio 0.70 (95 per cent c.i. 0.42 to 1.05; *P*= 0.082); R0 rate: 92.5 *versus* 86.5 per cent, *P*= 0.186). The 5-year OS rate was 62.5 (95 per cent c.i. 45.5 to 71.5) per cent for OLR and 64.3 (48.2 to 69.5) per cent for LLR. Longer duration of surgery, lower blood loss and morbidity, and shorter postoperative stay were found for LLR on postmatching analysis.

**Conclusion:**Propensity score matching showed that LLR for CRLM may provide R0 resection rates and long-term OS comparable to those for OLR, with lower blood loss and morbidity, and shorter postoperative hospital stay.

**+A: Introduction**

In the past decade a large number of studies have reported on the feasibility, safety and oncological efficacy of the laparoscopic approach in the management of primary and secondary liver lesions1,2. Many of these studies have highlighted the benefits of laparoscopic liver resections in terms of less intraoperative blood loss, lower morbidity rates, shorter postoperative stay and earlier return to functional activities. Some studies have even reported superior oncological results with the laparoscopic approach3.

These results have to be interpreted with caution owing to the potential role of selection bias and its effect on outcomes and conclusions. The majority of reports from which such data have been extracted are case series, case–control studies or meta-analyses of non-randomized studies2,4–6. Thus, the evidence in favour of the laparoscopic approach to liver resection was rated as low at the recent Second International Consensus Conference on Laparoscopic Liver Resections held in Iwate, Japan7. The need for a higher level of evidence in order to formulate recommendations is clear. So far, no randomized clinical trial on laparoscopic (LLR) *versus* open (OLR) liver resection has been completed. The Oslo CoMet trial is actively randomizing patients with resectable colorectal liver metastases (CRLM) to LLR or OLR, and is about to reach its recruitment target (NCT01516710). The multinational Orange II Plus trial, which has the same randomization, also includes patients with operable CRLM and recruitment is ongoing (NCT01441856). The Orange II trial (laparoscopic *versus* open left lateral sectionectomies in enhanced recovery after surgery) was stopped prematurely owing to slow accrual; its results are currently under review (NCT00874224).

The propensity score (PS) method has been referred to as a successful tool in minimizing treatment selection bias in the context of observational studies8. The balance that a randomized study is expected to create by design is here established by statistical adjustment. Provided suitable matching is performed, observational studies with PS matching may provide evidence comparable to that from randomized clinical trials9.

The present authors have previously reported their earlier experience on short- and mid-term outcomes of LLR *versus* OLR for CRLM10. Here, the short- and long-term oncological outcomes of a large cohort of patients are reported, and the role of PS matching analysis in eliminating bias when comparing the laparoscopic and open approaches is highlighted.

**+A: Methods**

*+B: Patient selection, indication for liver resection and surgical technique*

A prospectively collected, single-centre database of patients undergoing liver resections at Southampton University Hospital (August 2004 to April 2015) was reviewed. All consecutive liver resections performed for CRLM were selected. The operative strategy included the intention to achieve macroscopic negative margins with an estimated liver remnant volume to bodyweight ratio above 0.5 per cent11. For all patients, preoperative staging was completed with chest/abdominal CT and liver-specific MRI with triphasic contrast.

Exclusion criteria were the presence of concomitant extrahepatic liver metastases, synchronous colorectal resection of primary tumours, intraoperative or postoperative ablation (radiofrequency or microwave) and two-stage hepatectomy. The resulting cohort was divided into a laparoscopic group and an open group based on the approach to liver resection (prematching cohort). A purely laparoscopic procedure was attempted in all patients and no hybrid techniques were used. The surgical technique for laparoscopic left lateral sectionectomy, major formal hemihepatectomies and resections in posterosuperior segments has been described12–15. Open liver resections were routinely performed through a right subcostal J-shaped incision with the use of a LOTUS® (laparoscopic operation by tortional ultrasound) ultrasonic dissector (S.R.A Developments, Ashburton, UK) and CUSA® (Cavitron ultrasonic surgical aspirator; Integra, Plainsboro, New Jersey, USA). Vasculobiliary pedicles were managed with clips, ties or staplers according to location and size.

*+B: Endpoints*

The main endpoint of the study was to assess the short- and long-term oncological efficiency of laparoscopic liver resections compared with the open approach. This included evaluation of the completeness of resection (R0) as margin negativity is considered to have a major impact on disease-specific survival and postoperative hepatic recurrence rates. Resection margins were defined as R0 (microscopically more than 1 mm from resection margin) and R1 (microscopically less than 1 mm from resection margin)16. Long-term outcomes included overall survival (OS), recurrence-free survival (RFS) and disease-free survival (DFS), and their cumulative estimates at 1, 3 and 5 years. OS was estimated from liver resection until death; RFS was estimated from liver resection to the first documented recurrence of disease; and DFS was defined as survival from liver resection until incurable recurrence. Patients who did not experience the event (death, recurrence or incurable recurrence) were censored at their last follow-up date. Data were analysed according to the intention-to-treat principle.

Perioperative outcomes were also analysed for the assessment of feasibility and efficacy of the procedures. These included: duration of surgery (min), blood loss (ml), use of the Pringle manoeuvre (frequency and duration (min)), high-dependency unit (HDU) and total postoperative stay (days). Mortality and morbidity rates (general and liver-specific) were evaluated within 90 days of resection. The severity of postoperative morbidity was classified according to Dindo–Clavien17. Liver-specific complications were defined as: liver failure according to the ‘50–50 criteria’ on postoperative day 518; ascites as abdominal drainage output greater than 10 ml per kg bodyweight per day after postoperative day 319; and biliary leakage as a bilirubin concentration in the drainage fluid more than three times greater than serum total bilirubin level20.

*+B: Propensity score matching*

PS matching was performed on the initial cohort in order to adjust any difference in average outcomes for treatment selection bias.

For the purpose of this study, PS matching was performed by taking into account major observed confounders in the allocation of patients to laparoscopic or open liver resection21–24. Propensity scores were generated by logistic regression and relied on the following co-variables: age (less than 70 or 70 years or more), ASA fitness grade (I–II or III–IV), number of liver lesions (solitary or multiple), size of largest liver lesion (5 cm or less or more than 5 cm), number of concomitant liver resections (single or multiple), extent of liver resection (minor ormajor), tumour location (anterolateral or posterosuperior segments) and phase of surgical experience (earlier phase (2004–2009) or later phase (2010–2015)). Major hepatectomy was defined as the resection of three or more liver segments25.

After estimation of propensity scores, a regular 1 : 1 nearest-neighbour matching process was performed with inclusion of the following additional co-variables, given their potential influence on oncological outcomes24,26,27: administration of perioperative chemotherapy (yes or no), timing of metastatic disease (synchronous or metachronous), distribution of liver disease (unilobar or bilobar), location of primary tumour (colon or rectum) and lymph node status of the primary tumour (positive or negative). To improve balance, a small caliper (0.2) was specified. Neither replacement nor discarding of units was imposed. After matching, residual imbalance of co-variables was tested by univariable (standardized mean difference cut-off 0.25) and multivariable (Hansen and Bowers test; Iacus, King and Porro test) methods.

*+B: Statistical analysis*

Statistical analysis was performed using SPSS® version 22 (IBM, Armonk, New York, USA). Median (range) values were considered for continuous variables as distribution was skewed (Shapiro–Wilk test). For the prematching cohort, continuous and categorical variables were compared with the non-parametric Mann–Whitney *U* test and Fisher’s exact test, as appropriate. For the balanced cohort, continuous and categorical variables were compared using the Wilcoxon signed rank test and McNemar’s test respectively. Survival curves for RFS, DFS and OS were plotted by means of the Kaplan–Meier method. For the prematching cohort, comparison of survival probabilities was determined with the log rank (Mantel–Cox) test and a Cox proportional hazards model. For the balanced cohort, comparison of survival probabilities was determined using the Cox proportional hazards model, allowing for the matched nature of the data with shared frailty. Hazard ratios (HRs) were expressed with 95 per cent confidence intervals. Statistical significance was set at *P*< 0.050.

**+B: Results**

A total of 367 patients undergoing liver resection for CRLM met the inclusion criteria (laparoscopic approach, 176; open approach, 191) (*Table S1*, supporting information). More patients in the open group had multiple liver lesions (68.1 per cent *versus* 46.6 per cent in the LLR group; *P*< 0.001). In addition, patients undergoing open group were more likely to have a major liver resection (63.9 *versus* 37.5 per cent respectively; *P*< 0.001) and multiple concomitant resections (39.3 *versus* 27.8 per cent; *P*= 0.027).

After PS matching, 101 patients were excluded, leaving 266 for comparison in the balanced cohort (133 laparoscopic *versus* 133 open liver resection). Adequate balance between the two groups was attained, as all the selected co-variables had a mean difference of less than 0.25 (*Table 1*). Furthermore, Hansen and Bowers test for global imbalance was not significant (χ2 = 15.64, *P*= 0.336) and Iacus, King and Porro test was reduced in the matched sample, indicating that the overall balance after matching improved (L1 before matching, 0.921; L1 after matching, 0.886). The reduction of imbalance after PS matching is illustrated by histograms with overlaid kernel density estimates for mean difference (*Fig. S1*, supporting information).

Types of liver resection performed with the laparoscopic approach included: extended right hemihepatectomy (8 patients, 6.0 per cent), right hemihepatectomy (43 patients, 32.3 per cent), extended left hemihepatectomy (6, 4.5 per cent), left hemihepatectomy (8 patients, 6.0 per cent), left lateral sectionectomy (19, 14.3 per cent), right posterior sectionectomy (3, 2.3 per cent), bisegmentectomy (6 patients, 4.5 per cent), single non-anatomical resection (23 patients, 17.3 per cent) and multiple non-anatomical resection (17 patients, 12.8 per cent). Open liver resections included: extended right hemihepatectomy (22, 16.5 per cent), right hemihepatectomy (41 patients, 30.8 per cent), extended left hemihepatectomy (3, 2.3 per cent), left hemihepatectomy (5 patients, 3.8 per cent), left lateral sectionectomy (9, 6.8 per cent), right posterior sectionectomy (10, 7.5 per cent), bisegmentectomy (1, 0.8 per cent), single non-anatomical resection (24 patients, 18.0 per cent) and multiple non-anatomical resection (18, 13.5 per cent).

Thirteen (9.8 per cent) of the 133 patients in the laparoscopic group were converted to open surgery, leaving a total of 120 cases completed laparoscopically. Reasons for conversion were: concern for oncological inadequacy (5 patients), technical difficulty (3), bleeding (3) and intra-abdominal adhesions (2). According to the intention-to-treat design of the study, patients undergoing conversion were kept in the laparoscopic group for later analysis.

*+B: Perioperative outcomes*

Analysis of the prematching cohort revealed that laparoscopic liver resection was associated with longer duration of surgery (*P*= 0.024), less blood loss (*P*< 0.001) and more frequent Pringle manoeuvre (*P*< 0.001) (*Table 2*). Postoperative HDU and total stay were shorter in patients undergoing LLR *P* < 0.001 and *P*< 0.001 respectively), as and the morbidity rate was lower (general, *P*< 0.001; liver-specific, P = 0.001). Duration of Pringle manoeuvre (when adopted) and 90-day mortality rate was similar in the two groups. The above findings were confirmed at analysis on the balanced cohort (*Table 2*). A detailed description of the postoperative complications is provided in *Table S2* (supporting information.

*+B: Oncological outcomes*

Analysis of the prematching cohort showed a higher R0 resection rate in patients undergoing LLR (*P*= 0.030). However, in the balanced cohort the R0 resection rate was comparable between LLR and OLR (*P*= 0.186) (*Table 2*).

Kaplan–Meier survival curves are shown in *Figs 1–3*. The median length of follow-up was 23 and 30 months for patients undergoing OLR and LLR respectively. Longer median OS was seen for LLR in the prematching cohort (73.6 months (95 per cent c.i. 4-108) vs. 48.2 months (95 per cent c.i. 5-105) for LLR and OLR, respectively; Log Rank p = 0.047; hazard ratio 1.54 (95 per cent c.i. 0.67 – 1.89), p = 0.021) (*Fig. 1a*). The overall difference in 5-year OS rate was not confirmed in analysis of the balanced cohort (55.2 months (95 per cent c.i. 5-112) vs. 65.3 months (95 per cent c.i. 3-104) for LLR and OLR, respectively; hazard ratio 0.70 (95 per cent c.i. 0.42–1.05), p = 0.082) (*Fig. 1b*). Cumulative 1-, 3- and 5-year OS rates in patients undergoing OLR and LLR were 89.4, 68.9 and 62.5 (95 per cent c.i. 45.5 to 71.5) per cent, and 90.8, 76.8 and 64.3 (48.2 to 69.5) per cent, respectively.

Median RFS was similar between the two groups in both prematching (15.5 months (95 per cent c.i. 13-17) vs. 13.8 months (95 per cent c.i. 11-17) for LLR and OLR, respectively; Log Rank p = 0.178; hazard ratio 0.85 (95 per cent c.i. 0.77 – 1.28), p = 0.454) and balanced cohorts (16.2 months (95 per cent c.i. 11-19) vs. 15.8 months (95 per cent c.i. 15-20) for LLR and OLR, respectively; hazard ratio 0.88 (95 per cent c.i. 0.55–1.24), p = 0.238). (*Fig. 2*). Cumulative 1-, 3- and 5-year RFS rates in the OLR and LLR group were 58.7, 36.4 and 24.3 (95 per cent c.i. 12.3 to 46.6) per cent, and 60.5, 30.4 and 23.7 (14.4 to 41.8) per cent, respectively.

Median DFS was also similar between the two groups at analysis in both the prematching (35.3 months (95 per cent c.i. 23-45) vs. 41.7 months (95 per cent c.i. 28-48) for LLR and OLR, respectively; Log Rank p = 0.508; hazard ratio 0.88 (95 per cent c.i. 0.61 – 1.39), p = 0.296) and the balanced cohort (34.4 months (95 per cent c.i. 19-39) vs. 38.1 months (95 per cent c.i. 23-41) for LLR and OLR, respectively; hazard ratio 0.82, 95 per cent c.i. 0.67–1.55, p = 0.552) (*Fig. 3*). Cumulative 1-, 3- and 5-year DFS rates in the OLR and LLR group were 71.4, 53.0 and 52.5 (95 per cent c.i. 45.6 to 61.7) per cent, and 68.5, 44.1 and 35.8 (31.7 to 55.1) per cent, respectively.

Hepatic relapse occurred in 42 patients (31.6 per cent) in the laparoscopic group after a median of 15 months, compared with 36 patients (27.1 per cent) in the open group after a median of 18 months (*P*= 0.394). Recurrence at the transection edge was documented in one patient in each group. In the LLR group, half of these liver recurrences (21 of 42, 50 per cent) were treated with curative intent (repeated liver resection, 15; ablative treatment, 6). In the OLR group, 16 (44 per cent) of the 36 recurrences were treated with curative intent (repeated liver resection, 7; ablative treatment, 9). Extrahepatic recurrence occurred in 37 (27.8 per cent) of the 133 patients in the laparoscopic group and in 28 (21.1 per cent) of those in the open group. No port-site metastases were documented.

**+A: Discussion**

Recent literature1,2 has highlighted the benefits of LLR in terms of less intraoperative blood loss, lower morbidity rates, shorter postoperative stay and earlier return to functional activity compared with the traditional open approach. Some studies have even reported superior oncological results with use of the laparoscopic technique3. However, most of these reports were case series, case–control studies or meta-analyses of non-randomized studies2,4–6. Hence, selection biases cannot be excluded.

The present study reports the results of a single-centre experience in laparoscopic and open liver resection for CRLM before and after applying of the PS matching method. In this series, prematching median OS and R0 resection rate were better in patients undergoing LLR, potentially leading to the conclusion that more radical liver resections and, consequently, better long-term survival can be achieved compared with the open approach. However, when careful PS matching was implemented, a number of different results and conclusions were obvious. Indeed, differences in proportions of laparoscopic and open R0 resection were reduced after matching, resulting in a non-significant difference between the two groups. Similarly, in the balanced cohort OS was similar in open and laparoscopic groups.

Patient characteristics and surgeon preference are important factors in the allocation of patients to LLR or OLR21–23. Similarly, both clinical and biological factors have been identified as prognostic factors for disease-specific survival after liver resection in patients with CRLM26,27. In the present study, all major reported confounders in the allocation of patients to laparoscopic or open surgery for CRLM were taken into account, along with a number of factors influencing long-term oncological outcomes. The results obtained when analysing the matched groups suggest that oncological outcomes obtained with the laparoscopic approach are similar to those for open surgery. These findings were further bolstered by the comparable RFS and DFS after open and laparoscopic liver resection, and the similar incidence of hepatic relapse in both groups.

Lower blood loss and longer duration of surgery in patients undergoing LLR was observed on the prematching analysis and confirmed on analysis of the balanced cohort. Given the similar distribution of major and minor hepatectomies in the two matched groups, and the similar proportion of lesions located in posterosuperior segments, it seems reasonable to conclude that these are true intraoperative outcomes when the laparoscopic approach is applied in complex and major liver resections, and not only in minor resections.

Similarly, shorter HDU and total postoperative stay for patients undergoing LLR were confirmed on prematching and postmatching analysis. In addition, lower general and liver-specific morbidity rates were observed. These findings represent major advantages for patients. Indeed, in the modern era of the deployment of multimodality strategies for the management of CRLM, safe and faster postoperative recovery from surgery may favour a prompt start of adjuvant chemotherapy28.

A recent similar multicentre study from Japan29 showed comparable operating times for LLR and OLR. However, when analysing the types of resection included in that study, it is noteworthy that there was a low proportion of major hepatectomies, perhaps explaining the discrepancy with the present results. In addition, the postoperative morbidity rate was similar for LLR and OLR, and postoperative length of stay was longer than that in the present study. From an oncological point of view, the Japanese study was comparable with the present findings in revealing similar OS and R0 resection rates in the two groups. Comparison of the two studies is difficult, because the Japanese study was multicentre, involving a large number of centres and surgeons with different levels of experience using a variety of minimally invasive approaches (purely laparoscopic, hand-assisted and hybrid techniques).

The present results are from a large single-centre experience comparing LLR and OLR for CRLM before and after the implementation of PS matching. In addition, the advantage of having a large number of major and minor hepatectomies in both groups permitted PS matching on a normally distributed population, similar to that encountered in daily clinical practice in tertiary hepatobiliary centres. In view of the number of patients involved and the good balance achieved for both technical and oncological factors, the present results provide valuable evidence regarding the impact of the laparoscopic approach in the management of CRLM.

A known limitation of the PS matching process is the inability to account for unknown confounders that might have a significant impact on patients’ outcome. This is an issue that only an RCT will be able to overcome. Thus, results from the Oslo CoMet, Orange II Plus and Orange II trials are eagerly awaited.

**+A: Disclosure**

The authors declare no conflict of interest.

**+A: References**

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**Supporting information**

Additional supporting information may be found in the online version of this article:

**Fig. S1** Mean differences before and after matching (Word document)

**Table S1**Comparison of co-variables in the prematching cohort(Word document)

**Table S2**Postoperative morbidity in the balanced cohort classified according to Dindo–Clavien grading of surgical complications (Word document)

**<TYPESETTER: PLEASE FOLLOW MARK-UPS OF FIGS 1-3>**

**Fig. 1** Kaplan–Meier curves for overall survival following laparoscopic (LLR) and open (OLR) liver resection in **a** prematching and **b** balanced cohorts. **a** *P* = ??? **P = 0.047 (Log Rank Test) and P = 0.021 (Cox proportional hazards model)**, **b** *P* = ??? **P = 0.082** (??? test) **(Cox proportional hazards model with shared frailty).**

**Fig. 2** Kaplan–Meier curves for recurrence-free survival following laparoscopic (LLR) and open (OLR) liver resection in **a** prematching and **b** balanced cohorts. **a** *P* = ??? **P = 0.178 (Log Rank Test) and P = 0.454 (Cox proportional hazards model)**, **b** *P* = ??? **P = 0.238** (??? test) **(Cox proportional hazards model with shared frailty).**

**Fig. 3** Kaplan–Meier curves for disease-free survival following laparoscopic (LLR) and open (OLR) liver resection in **a** prematching and **b** balanced cohorts. **a** *P* = ??? **P = 0.508 (Log Rank Test) and P = 0.296 (Cox proportional hazards model)**, **b** *P* = ??? (??? test) **P = 0.552** (??? test) **(Cox proportional hazards model with shared frailty).**

**Table 1** Comparison of co-variables in the balanced cohort with mean differences after propensity score matching

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OLR (*n* = 133) | LLR (*n* = 133) | *P*\* | MD |
| Age (years) |  |  | 0.552 | 0.077 |
| ≤ 70 | 80 (60.2) | 85 (63.9) |  |  |
| > 70 | 53 (39.8) | 48 (36.1) |  |  |
| Sex |  |  | 0.734 | 0.060 |
| F | 50 (37.6) | 54 (40.6) |  |  |
| M | 83 (62.4 | 79 (59.4) |  |  |
| ASA fitness grade |  |  | 0.999 | 0.001 |
| I–II | 116 (87.2) | 116 (87.2) |  |  |
| III–IV | 17 (12.8) | 17 (12.8) |  |  |
| Phase of surgical experience |  |  | 0.899 | 0.041 |
| 2004–2009 (former) | 41 (30.8) | 43 (32.3) |  |  |
| 2010–2015 (latter) | 92 (69.2) | 90 (67.7) |  |  |
| Extent of liver resection |  |  | 0.865 | 0.093 |
| Minor | 62 (46.6) | 68 (51.1) |  |  |
| Major | 71 (53.4) | 65 (48.9) |  |  |
| No. of concomitant liver resections |  |  | 0.812 | 0.033 |
| Single | 83 (62.4) | 85 (63.9) |  |  |
| Multiple | 50 (37.6) | 48 (36.1) |  |  |
| No. of liver lesions |  |  | 0.724 | 0.030 |
| Solitary | 56 (42.1) | 54 (40.6) |  |  |
| Multiple | 77 (57.9) | 79 (59.4) |  |  |
| Size of biggest lesion (cm) |  |  | 0.468 | 0.055 |
| ≤ 5 | 106 (79.7) | 112 (84.2) |  |  |
| > 5 | 27 (20.3) | 21 (15.8) |  |  |
| Tumour location |  |  | 0.852 | 0.080 |
| Anterolateral segments | 88 (66.2) | 83 (62.4) |  |  |
| Posterosuperior segments | 45 (33.8) | 50 (37.6) |  |  |
| Location of primary (*n* = 119) |  |  | 0.120 | 0.135 |
| Colon | 53 (44.5)  **60 (45.1)** | 66 (55.5)  **73 (54.9)** |  |  |
| Rectum | 66 (55.5)  **73 (54.9)** | 53 (44.5)  **60 (45.1)** |  |  |
| Lymph node status of primary |  |  | 0.174 | 0.235 |
| Negative | 52 (39.1) | 37 (27.8) |  |  |
| Positive | 81 (60.9) | 96 (72.2) |  |  |
| Perioperative chemotherapy |  |  | 0.117 | 0.186 |
| No | 24 (18.0) | 39 (29.3) |  |  |
| Yes | 109 (82.0) | 94 (70.7) |  |  |
| Synchronous or metachronous metastases |  |  | 0.999 | 0.001 |
| Synchronous | 51 (38.3) | 51 (38.3) |  |  |
| Metachronous | 82 (61.7) | 82 (61.7) |  |  |
| Unilobar or bilobar disease |  |  | 0.476 | 0.092 |
| Unilobar | 103 (77.4) | 98 (73.7) |  |  |
| Bilobar | 30 (22.6) | 35 (26.3) |  |  |

Values in parentheses are percentages. OLR, open liver resection; LLR, laparoscopic liver resection; MD, mean difference. \*McNemar’s test.

**Table 2**Perioperative outcomes in prematching and balanced cohorts

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Prematching cohort | | |  | Balanced cohort | | |
| OLR (*n* = 191) | LLR (*n* = 176) | Difference†‡ | OLR (*n* = 133) | LLR (*n* = 133) | Difference†‡ |
| Duration of surgery (min)\* | 210 (80–900) | 240 (25–540) | 103 (90, 120) |  | 210 (90–900) | 295 (10–540) | 110 (80, 145) |
| *P* | 0.024§ | |  |  | < 0.001# | |  |
| Blood loss (ml)\* | 500 (50–5000) | 322 (10–2800) | 375 (350, 525) |  | 500 (50–4500) | 400 (10–2800) | 300 (200, 700) |
| *P* | < 0.001§ | |  |  | 0.040# | |  |
| Pringle manoeuvre | 70 (36.6) | 101 (57.4) | 21.1 (10.6, 30.8) |  | 50 (37.6) | 86 (64.7) | 27.1 (15.5, 37.6) |
| *P* | < 0.001¶ | |  |  | < 0.001\*\* | |  |
| Pringle manoeuvre (min)\* | 30 (4–72) | 30 (3–94) | 22.5 (−8, 40) |  | 27.5 (5–72) | 35 (3–94) | 16 (−8, 30) |
| *P* | 0.200§ | |  |  | 0.349# | |  |
| HDU stay (days)\* | 2 (0–48) | 1 (0–10) | 1 (1, 2) |  | 2 (0–48) | 1 (0–10) | 1 (1, 1) |
| *P* | < 0.001§ | |  |  | < 0.001# | |  |
| Total stay (days)\* | 7 (2–150) | 4 (1–57) | 4 (3, 5) |  | 7 (2–150) | 4 (1–57) | 4 (3, 4) |
| *P* | < 0.001§ | |  |  | < 0.001# | |  |
| Morbidity | 78 (40.8) | 38 (21.6) | −19.3 (−28.1, −10.8) |  | 53 (39.8) | 31 (23.3) | −16.5 (−26.7, 5.8) |
| *P* | < 0.001¶ | |  |  | 0.002\*\* | |  |
| Liver-specific morbidity | 39 (20.4) | 14 (8.0) | −12.5 (−5.25, −19.8) |  | 26 (19.5) | 12 (9.0) | −10.5 (−19, 1.9) |
| *P* | 0.001¶ | |  |  | 0.012\*\* | |  |
| 90-day mortality | 2 (1.0) | 1 (0.6) | −0.6 (−3.5, 2.1) |  | 2 (1.5) | 1 (0.8) | −0.7 (−4.6, 2.8) |
| *P* | 0.999¶ | |  |  | 0.999\*\* | |  |
| R0 resection | 167 (86.4)  **(87.4)** | 166 (94.3) | 7.9 **6.9** (1.7, 14.4) |  | 115 (86.5) | 123 (92.5) | 6 (−1.9, 13.9) |
| *P* | 0.030¶ | |  |  | 0.186\*\* | |  |

Values in parentheses in open (OLR) and laparoscopic (LLR) liver resection columns are percentages unless indicated otherwise; \*values are median (range). †Values in parentheses are 95 per cent confidence intervals. ‡Median difference for continuous variables and difference in proportions for dichotomous categorical variables. HDU, high-dependency unit. §Mann–Whitney *U* test, ¶Fisher’s exact test, #Wilcoxon signed rank test and \*\*McNemar’s test.