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A prospective randomised controlled trial of laparoscopic *vs* open radical cystectomy for bladder cancer: perioperative and oncologic outcomes with 5-year follow-upT Lin *et al*

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Background: Laparoscopic radical cystectomy (LRC) is increasingly being used for muscle-invasive bladder cancer. However, high levels of clinical evidence comparing laparoscopic *vs* open radical cystectomy (ORC) are lacking.

Methods: A prospective randomised controlled clinical trial comparing LRC *vs* ORC in patients undergoing radical cystectomy for bladder cancer. Thirty-five patients were eligible for final analysis in each group.

Results: The median follow-up was 26 months (range, 4–59 months) for laparoscopic *vs* 32 months (range, 6–60 months) for ORC. Significant differences were noted in operative time, estimated blood loss (EBL), blood transfusion rate, analgesic requirement, and time to resumption of oral intake. No significant differences were noted in the length of hospital stay, complication rate, lymph node yield (14.1 ± 6.3 for LRC and 15.2 ± 5.9 for ORC), positive surgical margin rate, postoperative pathology, or recurrence rate (7 for LRC and 8 for ORC). The 5-year recurrence-free survival with laparoscopic *vs* ORC was 78.5% *vs* 70.9%, respectively ($P = 0.773$). The overall survival with laparoscopic *vs* ORC was 73.8% *vs* 67.4%, respectively ($P = 0.511$).

Conclusion: Our study demonstrated that LRC is superior to ORC in perioperative outcomes, including EBL, blood transfusion rate, and analgesic requirement. We found no major difference in oncologic outcomes. The number of patients is too small to allow for a final conclusion.

Although open radical cystectomy (ORC) and pelvic lymphadenectomy remain the gold standard treatment for muscle-invasive bladder cancer and high-risk recurrent noninvasive bladder cancer, there is increasing interest in laparoscopic radical cystectomy (LRC) and robot-assisted radical cystectomy. LRC may provide certain advantages in terms of blood loss, analgesic requirements, reduced scarring, and recovery. Studies of robot-assisted radical cystectomy also demonstrated its feasiblity and potential benefits of decreased blood loss (Nix *et al*, 2010; Parekh *et al*, 2012). However,

because of the lack of adequate comparative data and sufficient follow-up to demonstrate similar oncologic outcomes compared with traditional ORC, there remains significant scepticism about the true benefits of MIRC (Challacombe *et al*, 2011).

Currently, high levels of clinical evidence with respect to the long-term oncologic results of MIRC are limited in the peer-reviewed literature. Most reports are retrospective comparative studies (Hemal and Kolla, 2007; Porpiglia *et al*, 2007; Ha *et al*, 2010; Yu *et al*, 2012) or case series studies (Haber and Gill, 2007;

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Gillion *et al*, 2011), which represent significant selection bias. Herein, we present the perioperative complications, ileal neobladder function, and medium-term survival of a prospective randomised controlled clinical trial (RCT) comparing LRC *vs* ORC.

PATIENTS AND METHODS

All patients provided written informed consent, and were eligible for random assignment to either laparoscopic or open-surgery groups. This trial was approved by our local institutional ethical committee, and was conducted in accordance with good clinical practices and the Declaration of Helsinki. This study was funded by Sun Yat-Sen University Clinical Research 5010 Program, and was registered in Chinese Clinical Trial Registry (http://www.chictr.org/cn/, No: ChiCTR-TRC-10001003).

Patient selection. The inclusion criteria were (1) muscle-invasive bladder cancer T2–4a, N0–Nx, M0; (2) high-risk and recurrent non-–muscle-invasive tumours; (3) T1G3; and (4) extensive non-muscle-invasive disease that could not be controlled by transurethral resection and intravesical therapy. The exclusion criteria were (1) patient elected not to participate; (2) the presence of contraindications to radical cystectomy, including distant metastasis, an American Society of Anaesthesiologists score >3, and severe cardiac or pulmonary disease; (3) the presence of contraindications to neobladder, including urethral tumour, urethral stricture, abnormal abdominal straining, and decompensated renal function.

The preoperative evaluation included complete blood count, blood biochemistry, urine cytology, and computed tomography. Diagnostic transurethral resection and pathologic examination were performed in patients with invasive bladder cancer.

Randomisation. Patients were randomly assigned 1:1 at the preoperative assessment to receive either laparoscopic or open surgery at the time of preoperative assessment. Random numbers were computer generated by a statistician (J Zhang), and patients were stratified according to sex, age, and clinical stage.

Surgical technique. The surgical procedure was the same in the two groups except for the surgical approach. Our surgical techniques for LRC, bilateral PLND, and extracorporeal diversion have been previously described in detail (Huang *et al*, 2008). A five-port, fan-shaped transperitoneal approach was used, and bilateral PLND was performed first. The boundaries of a standard PLND were the bifurcation of the common iliac artery proximally, the genitofemoral nerve laterally, the circumflex iliac vein and lymph node of Cloquet distally, and the hypogastric vessels posteriorly, including the obturator fossa. Patients with a preoperative evaluation of T3 to T4a disease underwent extended PLND, in which the proximal extent of the dissection was the aortic bifurcation.

The peritoneum of the rectovesical pouch in men (Douglas pouch in women) was incised transversely, and the ampullae of the vas deferens were transected bilaterally. The dissection was along the dorsal side of the seminal vesicles. The seminal vesicles were not dissected but were left en bloc with the bladder. Denonvilliers' fascia was incised, and Denonvilliers' space between the rectum and the prostate was developed. An inverted U-shaped peritoneotomy was made to expose the anterior bladder wall and Retzius' space, and the endopelvic fascia was incised bilaterally. The puboprostatic ligament was dissected, and the dorsal vein complex was suture ligated.

Both ureters were ligated and transected with a LigaSure (Covidien, Boulder, CO, USA) just outside the bladder. The lateral pedicles of the bladder and the prostate were bilaterally divided

with the LigaSure, and the apex of the prostate was dissected using scissors. The specimen was placed in an endobag and immediately extracted through a 5-cm midline incision in the lower abdomen. The construction of an M-shaped ileal neobladder and ureteral reimplantation using a ureteral split-nipple technique was performed extracorporeally. Vesicourethral anastomosis was performed intracorporeally with a running-suture technique under laparoscopic visualisation.

Prophylactic antibiotic was given 30 min preoperatively. An additional dose was given when the operative time exceeded 3 h. Postoperative antibiotic administration was discontinued unless evidence of infection persisted. All surgeries were performed by a single surgeon (J. Huang), experienced in more than 100 cases of LRC and also experienced in ORC before this trial (Huang *et al*, 2008, 2010).

Pathological analysis and adjuvant therapy. All specimens were analysed according to the TNM classification (2002 Union Internationale Contre le Cancer) and graded by the 1973 World Health Organization classification. Pathologic subgroups were defined as organ confined ($\leqslant$pT2) and non-organ confined ($\geqslant$pT3) as well as lymph node negative and positive. Adjuvant chemotherapy was administered to patients with non-organ-confined or lymph node-positive disease with a gemcitabine and cisplatin combination chemotherapy regimen (Pectasides *et al*, 2005).

Follow-up scheme. Postoperative follow-up was conducted at 3-month intervals during the first year, at 6-month intervals during the second year, and annually thereafter. Follow-up visits consisted of a history, physical examination, and routine biochemical profile. Ultrasonography of the abdomen, urography, and chest X-rays was performed at 3, 6, and 12 months postoperatively, then annually unless otherwise clinically indicated. Abdominal/pelvic computed tomography scans were performed 6 months postoperatively and annually thereafter. Bone scans were performed when clinically indicated. We updated the survival status of all patients through telephone contact in February 2013.

Outcomes. Several outcomes were used when comparing the two groups. We assessed the following perioperative outcomes: operative time, estimated blood loss (EBL), analgesic requirement, time to resumption of oral intake, postoperative length of stay (LOS), and complication rate. All surgical complications were classified according to the Clavien classification system (Clavien *et al*, 2009). We also assessed neobladder functional outcomes; and oncologic outcomes such as LN yield, positive surgical margin rate (PSM), recurrence-free survival (RFS), and overall survival.

Statistical analysis. This trial was designed as a randomised non-inferiority single-centre study (Fueglistaler *et al*, 2007). The primary end point by which the sample size was determined was LN yield. Assuming the mean difference of LN yield between the two groups was 2 with a standard deviation of 4, a lost to follow-up proportion of 5%, and with a power of 80% at a significance level of 5% (two-tailed Student's *t*-test), 70 patients were enrolled in this trail.

Analyses were conducted following the intention-to-treat principle, with all randomised patients analysed according to their assigned treatment group. Categorical variables were analysed with the χ^2 test or Fisher's exact test as appropriate. Continuous variables were compared with the Student's *t*-test or the Mann–Whitney *U*-test as appropriate. Survival curves were estimated using the Kaplan–Meier method, and differences were compared with the log-rank test. Univariate and multivariable analysis of survival outcomes were conducted using Cox regression analysis, taking into account randomised procedure, age, LN status, and tumour pT stage. All *P*-values were two-sided and $P < 0.05$ was

considered statistically significant. All analyses were conducted using SPSS v.19.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Between 16 January 2008 and 30 November 2011, 73 patients were randomly assigned to either laparoscopic or open surgery. Three patients were excluded for tumour invasion of the urethra, and subsequently underwent the Bricker conduit procedure. A total of 35 patients in each group who underwent radical cystectomy and M-shaped ileal neobladder were included in the final analysis. Figure 1 presents the flowchart. The two treatment groups were homogeneous in terms of preoperative characteristics and clinical stages, as shown in Table 1. The median follow-up was 26 (4–59) months in the laparoscopic group, and 32 (6–60) months in the open-surgery group ($P = 0.972$). Three patients in each group were lost to follow-up, and they were included in the analysis but censored at the point of last follow-up.

Perioperative outcomes. The results of the perioperative outcomes are listed in Table 2. Operative time was significantly longer (282 *vs* 235 min; $P < 0.001$); blood loss was significantly lower (median 215 *vs* 510 ml; $P < 0.001$); analgesic requirement was significantly less (morphine equivalents, 12.6 *vs* 19.3 mg; $P < 0.001$), and the mean time to resumption of oral intake was significantly shorter (3.8 *vs* 4.8 d; $P = 0.001$) comparing LRC with ORC. Blood transfusions were given to 2 patients (both are intraoperative) in LRC and 12 patients (10 intraoperative, 2 postoperative) in ORC ($P = 0.003$).The mean postoperative length of stay was 15.8 days for LRC compared with 16.4 days in ORC, and this difference was not statistically significant ($P = 0.667$). No patient was converted to open surgery in the laparoscopic group and no perioperative mortality was observed in either group.

Table 1. Baseline characteristics of the patients and tumours

Category	LRC ($n = 35$)	ORC ($n = 35$)	*P* value
Mean age, mean ± s.d., years	63.2 ± 9.1	63.6 ± 8.9	0.851[a]
Sex, No.			
Male	32	32	1.0[b]
Female	3	3	—
BMI, mean ± s.d., kg m^{-2}	22.0 ± 2.7	22.9 ± 3.1	0.414[a]
Previous abdominal surgery, No.	3	5	0.707[b]
ASA grade, No.			
II	28	25	0.403[b]
III	7	10	—
Clinical stage, No.			
cT1	5	4	0.873[b]
cT2	23	25	—
cT3	7	6	—
Concomitant CIS, No.	1	2	1.0[b]
Tumour history, No.			
Primary tumour	25	28	0.403[b]
Recurrent after TURBT and/or partial cystectomy	10	7	—
Follow-up, median (range), months	26 (4–59)	32 (6–60)	0.972[c]
Lost to follow-up, No.	3	3	1.0[b]

Abbreviations: ASA = American Society of Anesthesiologists; BMI = body mass index; CIS = carcinoma *in situ*; LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; TURBT = transurethral resection of bladder tumour.
[a]Student's *t*-test.
[b]χ^2 test or Fisher's exact test.
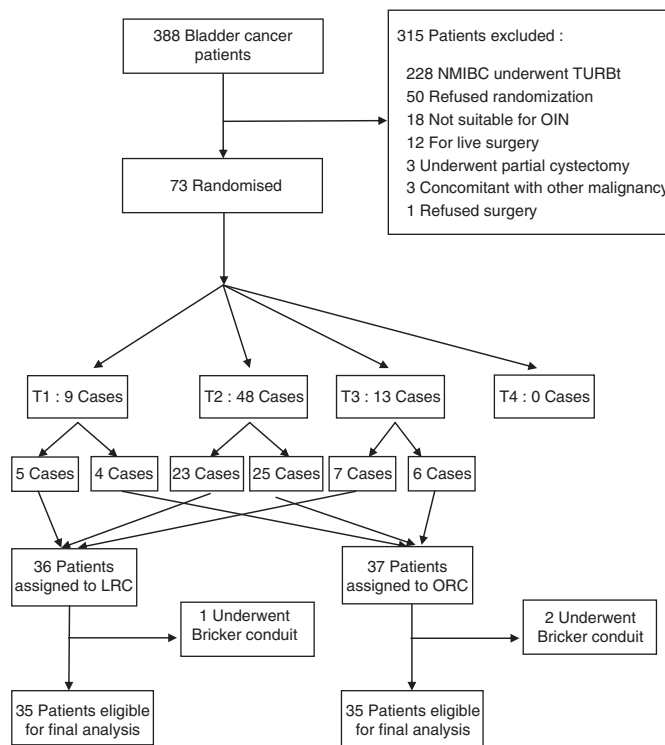[c]Mann–Whitney *U*-test.

Figure 1. Flow chart of patients. Abbreviations: LRC = laparoscopic radical cystectomy; NMIBC = non-muscle-invasive bladder cancer; OIN = orthotopic ileal neobladder; ORC = open radical cystectomy; TURBt = transurethral resection of bladder tumour.

Table 2. Perioperative outcomes

Category	LRC (n = 35)	ORC (n = 35)	P value
Operative time, min	282 ± 51	235 ± 34	<0.001[a]
PLND	84 ± 24	51 ± 17	<0.001[a]
Cystectomy	67 ± 18	56 ± 16	0.013[a]
OIN making	77 ± 22	74 ± 22	0.627[a]
OIN-urethra anastomosis	34 ± 9	25 ± 8	<0.001[a]
Estimated blood loss, ml	215 (55–810)	510 (105–1700)	<0.001[b]
Blood transfusions, No.	2	12	0.003[c]
Intraoperative	2	10	
Postoperative	0	2	
Analgesic requirement, mg (morphine equivalents)	12.6 ± 5.2	19.3 ± 6.3	<0.001[a]
Resumption of oral intake, d	3.8 ± 1.1	4.8 ± 1.2	0.001[a]
Postoperative LOS, d	15.8 ± 5.5	16.4 ± 6.1	0.667[a]
Conversion to ORC, No.	0	—	—
Perioperative mortality, No.	0	0	1.0[c]

Abbreviations: LOS = length of hospital stay; LRC = laparoscopic radical cystectomy; OIN = orthotopic ileal neobladder; ORC = open radical cystectomy; PLND = pelvic lymph node dissection.
[a]Student's t-test.
[b]Mann–Whitney U-test.
[c]χ^2 test or Fisher's exact test.

Table 3. Surgical complications stratified by the Clavien classification system

Complications (Clavien units)	LRC (n = 35)	ORC (n = 35)	P value
Grade II, No. (%)	20 (57.1%)	24 (68.6%)	0.322[a]
Urinary tract infection	1	2	—
Blood transfusion	2	12	—
Ileus	4	4	—
Lymphatic leakage	6	2	—
Delirium	2	0	—
Infectious peritonitis	0	1	—
Vesico-urethral anastomotic leakage	1	2	—
Uretero-pouch anastomotic leakage	2	0	—
Neobladder leakage	2	1	—
Grade IIIa, No. (%)	1 (2.9%)	3 (8.6%)	0.607[b]
Incisional haematoma	0	2	—
Rupture of incision required II stage suture	1	1	—
Grade IIIb, No. (%)	2 (5.7%)	4 (11.4%)	0.669[b]
Intraoperative damage of external iliac vessels	1	1	—
Abdominal-pouch fistula	0	1	—
Colon-pouch fistula	1	1	—
Ileo-pouch fistula	0	1	—

Abbreviations: LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy.
[a]χ^2 test.
[b]Fisher's exact test.

Complications. Complications graded by the Clavien classification system are summarised in Table 3. There was no significant difference in grade II ($P = 0.322$) complications between LRC and ORC. There was also no significant difference between LRC and ORC ($P = 0.607$ and $P = 0.669$, respectively) for grade IIIa and IIIb complications requiring surgical intervention.

Pathologic outcomes. Postoperative pathologic outcomes are presented in Table 4. There was no significant difference when comparing all pathologic categories between LRC and ORC. PSM was observed in one patient in each group. The mean numbers of LN yield were 14.1 in LRC and 15.2 in ORC ($P = 0.467$) and the positive LN rate was 22.9% (8/35) in both groups. The most common histologic type was transitional cell carcinoma (TCC, 97.1% in both groups), but seven patients were diagnosed with TCC with squamous differentiation (5.7%, 2/35 in LRC), glandular differentiation (2.9%, 1/35 in LRC), or coexisting prostate cancer (5.7%, 2/35 in each group). Bladder cancer in six patients in LRC (17.1%) and eight (22.9%) patients in ORC was associated with non-organ-confined diseases.

Neobladder function. Table 5 summarises the results of the ileal neobladders function 1 year after surgery, and no statistically significant difference was found between the two groups. The daytime continence rate was 89.3% in LRC and 86.7% in ORC ($P = 1.0$). The nighttime continence rate was 78.6% in LRC and 70% in ORC ($P = 0.456$). The median functional capacity was 305 ml in LRC and 325 ml in ORC ($P = 0.489$). There was no statistically significant difference regarding the number of patients with residual urine, their amount of residual urine, and the incidence of infected urine. Two patients in LRC and one patient in ORC could not void, and they required clean intermittent catheterisation four to six times a day to empty their ileal neobladders.

Survival outcomes. Local recurrence and distant metastases occurred in seven patients in LRC compared with eight patients in ORC ($P = 0.937$; Table 4).

As shown in Figures 2A and B, there was no significant difference in RFS ($P = 0.773$) and overall survival ($P = 0.551$) between LRC and ORC. The difference in RFS remained not statistically significant when restricting analyses to LN-negative patients ($P = 0.279$; Figure 2C) and LN-positive patients ($P = 0.542$; Figure 2D). We also analysed RFS according to LN status and pT stage and found that LN-negative patients were associated with a statistically significantly better RFS than LN-positive patients ($P < 0.001$; Figure 2E). Organ-confined patients were associated with a statistically significantly better RFS than non-organ-confined patients ($P < 0.001$; Figure 2F).

In univariate analyses, surgical technique ($P = 0.773$) was not associated with RFS, but age group ($P = 0.043$), LN status ($P < 0.001$), and pT stage ($P < 0.001$) were associated with RFS. The results of multivariate analyses were similar to the results of the univariate analyses except that LN status ($P = 0.133$) was not associated with RFS.

DISCUSSION

The primary aim of radical cystectomy for bladder cancer is to remove the primary tumour safely and completely, to perform adequate PLND, to achieve negative margins, and to provide optimal long-term survival and quality of life (Hemal and Kolla, 2007). Although ORC remains the standard treatment for bladder cancer, it is associated with significant morbidity even when performed by experienced surgeons, in part, because of the long incision, prolonged abdominal wall retraction, prolonged exposure of the peritoneal surface with major fluid shifts and poor vision, particularly in the deep pelvis and retrovesical area (Chang et al, 2001).

Table 4. Pathologic outcomes and sites of metastases			
Category	LRC (*n* = 35)	ORC (*n* = 35)	*P* value
Positive margins, No. (%)	0	1 (2.9%)	1.0[a]
Lymph node yield, No.			
Mean ± s.d.	14.1 ± 6.3	15.2 ± 5.9	0.467[b]
Median (range)	12 (4–32)	14 (5–25)	0.261[c]
LN status, No. (%)			
Positive	8 (22.9%)	8 (22.9%)	1.0[a]
Negative	27 (77.1%)	27 (77.1%)	—
Histologic type, No.			
TCC	29	32	0.273[a]
TCC with squamous differentiation	2	—	—
TCC with glandular differentiation	1	—	—
TCC coexisting prostate cancer	2	2	—
Squamous cell carcinoma	—	1	—
Carcinosarcoma	1	—	—
pT stage, No.			
pT1	8	7	0.935[a]
pT2	21	20	—
pT2a	14	12	—
pT2b	7	8	—
pT3	5	7	—
pT3a	4	2	—
pT3b	1	5	—
pT4a	1	1	—
Grade, No.			
Grade 1	4	3	0.511[a]
Grade 2	15	16	—
Grade 3	15	12	—
Unclassified	1	4	—
Concomitant CIS, No.	2	3	1.0[a]
Sites of recurrence	7 (20%)	8 (22.9%)	0.937[a]
Local recurrence	3 (8.6%)	3 (8.6%)	—
Distant metastases	4 (11.4%)	5 (14.3%)	—
Lung	2	3	—
Brain	—	1	—
Bone	2	1	—

Abbreviations: CIS = carcinoma *in situ*. LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy; TCC = transitional cell carcinoma.
[a]χ^2 test or Fisher's exact test.
[b]Student's *t*-test.
[c]Mann-Whitney *U*-test.

Table 5. Neobladder functional outcomes 12 months after surgery			
Category	LRC (*n* = 28)	ORC (*n* = 30)	*P* value
Daytime continent, No. (%)	25 (89.3)	26 (86.7)	1.00[a]
Nighttime continent, No. (%)	22 (78.6)	21 (70)	0.456[a]
Functional capacity, ml	305 (155–660)	325 (170–730)	0.489[b]
Patients with residual urine, No. (%)	11 (39.3%)	8 (26.7%)	0.306[a]
Residual urine volume, ml	60 (10–145)	45 (15–115)	0.310[b]
Infected urine, No. (%)	7 (25%)	5 (16.7%)	0.434[a]
Patients on clean intermittent catheterization, No. (%)	2 (7.1%)	1 (3.3%)	0.951[a]

Abbreviations: LRC = laparoscopic radical cystectomy; ORC = open radical cystectomy.
[a]χ^2 test or Fisher's exact test.
[b]Mann–Whitney *U*-test.

et al, 2011), where 171 patients had an orthotopic ileal neobladder reconstruction with a median follow-up of 37 months (maximum: 7 years), with encouraging oncologic outcomes. Nevertheless, these reports are susceptible to significant selection biases in which only the most favorable candidates underwent the laparoscopic procedure. Higher levels of evidence such as those with RCT are still needed. Therefore, we conducted this prospective, randomised trial of LRC *vs* ORC beginning in January 2008, with a maximum follow-up of 5 years. The baseline characteristics of the patients and tumours were well matched. Also, all patients underwent radical cystectomy by a single surgeon, who was experienced in both LRC and ORC. Therefore, we minimised the bias introduced by patient selection and surgeon, and provided sound evidence comparing LRC and ORC.

The perioperative outcomes of this study showed that the operative time was significantly longer, but EBL, analgesic requirement, and time to oral intake were significantly lower in LRC compared with ORC. These findings are similar to those of previous studies (Hemal and Kolla, 2007; Guillotreau *et al*, 2009). In our institution, the gastrostomy tube was removed after the patient passed flatus or stool and oral intake was then restarted with a liquid diet. Therefore, the time to resumption of oral intake seems longer compared with other centres, where cystectomy patients are allowed to drink on the day of open surgery and have a liquid diet on the first postoperative day (fast track surgery; Roth *et al*, 2013). As a result, the difference observed in the resumption of oral intake in our study should not be overemphasised.

Despite the longer operative time in LRC, its complication rate was not higher than ORC. According to Challacombe *et al* (2011), major (Clavien grade III-IV) complication rates ranged from 10 to 13% in LRC. Shabsigh *et al* (2009) analysed complications in 1142 ORC patients, and found a major complication rate of 13%. In our trial, we did not find a high rate of complications specific to the laparoscopic approach, such as uretero-pouch anastomotic leakage and neobladder leakage. This may be because our surgeon was very experienced in LRC. Also, ileal neobladders were constructed extracorporeally, which is a safe and effective way to decrease operative time and surgical complications (Hemal *et al*, 2008).

Bilateral PLND is important for both accurate staging and adequate local and regional control (Abol-Enein *et al*, 2011). Several studies have taken LN yield as an indicator of surgical quality with cystectomy (Huang and Stein, 2007; Nix *et al*, 2010). LRC must be able to replicate the standardised PLND possible with open surgery to be established as an alternative technique (Challacombe *et al*, 2011). Based on this premise, we used LN yield as the basis for sample size calculation and to serve as the primary end point for statistical comparison between laparoscopic
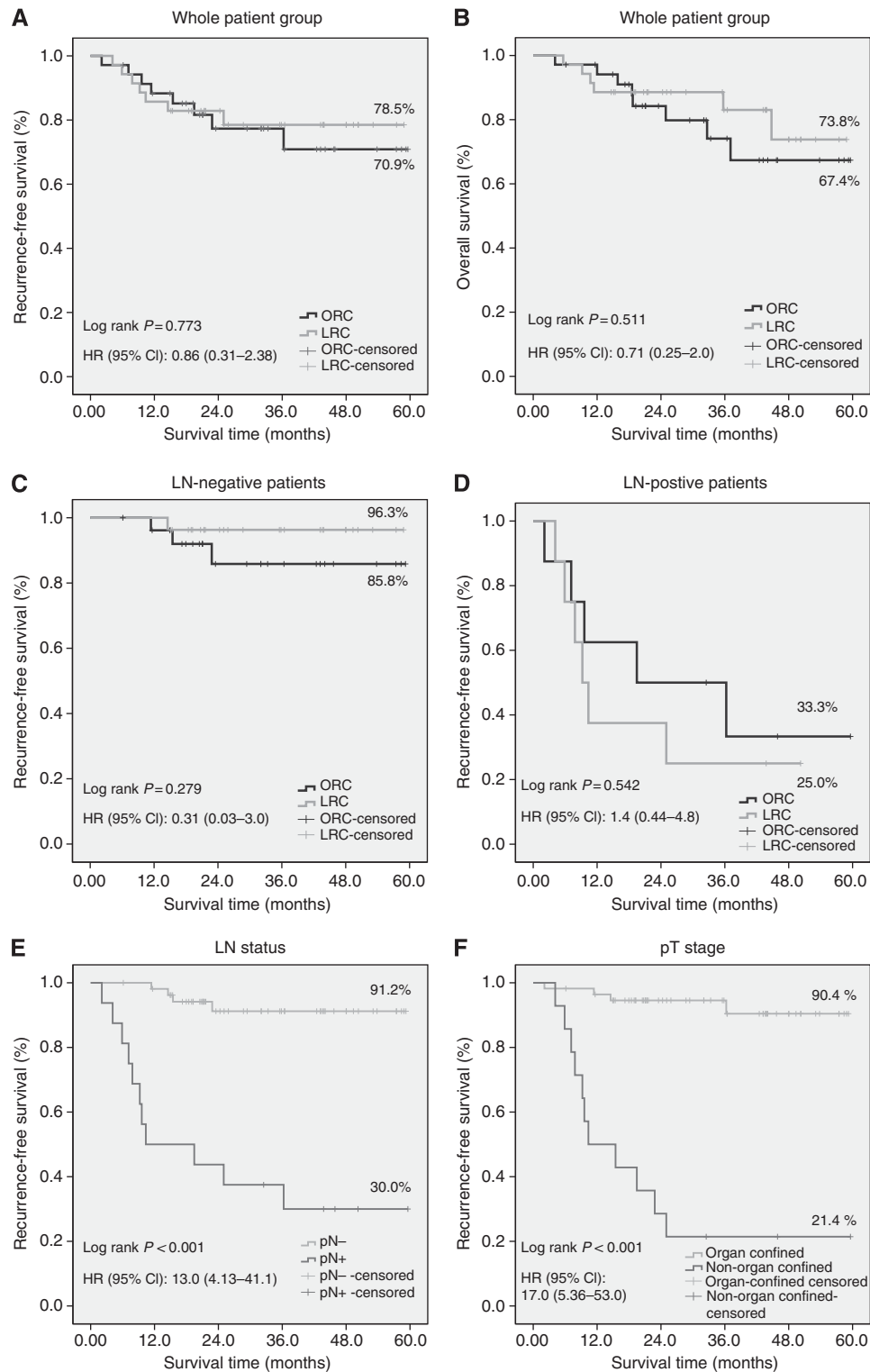
Since the first laparoscopic simple cystectomy reported by Parra *et al* (1992) 20 years ago, the minimal invasiveness of LRC in terms of reduced blood loss have made this procedure increasingly popular in the field of urology. However, what remains paramount is the long-term oncologic efficacy of LRC. Although the oncologic safety of laparoscopic surgery has not been proven inferior to open surgery in the treatment of other malignancies such as colon cancer and rectal cancer (Group TCOoSTS, 2004; Buunen *et al*, 2009; Lujan *et al*, 2009), the oncologic efficacy evidence of LRC for bladder cancer remains limited.

Several retrospective comparative studies (Hemal and Kolla, 2007; Porpiglia *et al*, 2007; Ha *et al*, 2010) and case series (Haber and Gill, 2007; Gillion *et al*, 2011) from major institutions have shown good early oncologic results over the initial 2–3 years (and in some patients up to 5 years) with low morbidity. Our institution reported the largest series of LRC (Huang *et al*, 2010; Challacombe

Figure 2. Kaplan–Meier curves for comparison of (**A**) recurrence-free survival (RFS) between laparoscopic radical cystectomy (LRC) and open radical cystectomy (ORC), (**B**) overall survival between LRC and ORC, (**C**) RFS in lymph node (LN)-negative patients, (**D**) RFS in LN-positive patients, (**E**) RFS according to LN status, (**F**) RFS according to pT stage. Abbreviations: CI = confidence interval; HR = hazards ratio.

vs open approaches. Our result showed that LN yield in LRC was not inferior to ORC. In previous LRC series studies (Haber *et al*, 2008), the mean number of lymph nodes retrieved was 15.5 (range, 2–49), which was consistent with our study. Retrospective comparative studies (Hemal and Kolla, 2007; Porpiglia *et al*, 2007) also showed no statistically significant difference in LN yield between LRC and ORC.

PSM is an independent predictor of metastatic progression in patients undergoing radical cystectomy, which reportedly increased the risk of metastatic progression at 5 years from 32 to 74% (Dotan *et al*, 2007). According to Chade *et al* (2010), the incidence of PSM ranged from 4 to 5% of the ORC cases, and from 0 to 5% of the LRC cases. In our trial, the PSM rate was 2.9% (1/35) in both groups. These two patients' pathologic stage was pT3b. Dotan *et al* (2007)

reported that none of the patients with organ-confined disease had evidence of PSM, suggesting that tumour infiltration may be the main limitation in achieving a negative margin.

Port-site metastasis is another debated issue for LRC. In our previous LRC series study including 171 patients (Huang *et al*, 2010), only 1 patient with grade 3 pT3N1M0 TCC developed port-site seeding. In the present trial, no port-site metastasis occurred. No port-site metastasis was found in other studies of LRC (Haber and Gill, 2007; Hemal and Kolla, 2007; Porpiglia *et al*, 2007; Guillotreau *et al*, 2009; Ha *et al*, 2010). Generally, port-site metastasis is a rare event in LRC. Improved techniques, including gentle clamping and entrapping of LNs and specimens into a secured endobag before extraction, could minimise the risk. Our results showed that LRC can achieve a low risk of tumour dissemination, and our results are reproducible by following the principles of oncologic surgery: do not transgress the tumour boundaries, ensure adequate margins during the resection, immediately close the bladder neck and prostate apex once opened, and avoid any bladder wall perforation to prevent potential spillage of cancer cells (Cathelineau *et al*, 2005).

Long-term survival is the final touchstone for the oncologic efficiency of LRC. A large ORC series by Stein *et al* (2001) demonstrated a 5-year RFS of 68%. RFS results varied most widely at 2–3 years in previous LRC reports with rates of 60–85% (Chade *et al*, 2010). Two retrospective comparative studies (Hemal and Kolla, 2007; Ha *et al*, 2010) showed no significant difference in 3-year RFS and overall survival between LRC and ORC. In the present study, we also observed similar RFS and overall survival in two treatment groups. However, a final conclusion is not possible because both groups were having mainly low-risk patients as expressed and reflected by the small number of events.

Our study has the following limitations: first, both the patients and the surgeons could not be blinded because of the surgical nature of the trial. Second, our patient numbers were relatively small and our study was a single-institution study. The basis for the statistical analysis (non-inferiority) was a possible difference in the LN yield. However, most of the other end points did not have enough events to conclude non-inferiority. Another limitation is that we primarily included patients with organ-confined disease. Indeed, only six patients were stage pT3b, and five of them were in the open group. Therefore, it is not surprising that the PSM as well as the oncological outcome, especially for the laparoscopic group, showed favourable results with respect to PSM or survival. The only patient with stage pT3b in the laparoscopic group did have PSM. It is unknown whether the outcome would be less favourable for the laparoscopic group if more high-risk patients for PSM were included. Also, despite the maximum follow-up of this trial of nearly 5 years, the median follow-up was only approximately 2 years. Therefore, future RCTs with large sample sizes and longer follow-ups are necessary to provide more convincing survival outcomes.

One of the strong points of this study is that the same surgeon (J Huang) performed LRC and ORC. Before running this randomised trial, he performed more than 100 LRCs. Thus, the results achieved by this single surgeon should not be over-interpreted. Rather it shows that the dedicated front runner for laparoscopic surgery is able—after a long run in phase—to achieve results comparable to ORC. However, this does not mean that laparoscopic surgery in general is equivalent to open surgery. It requires more skill, more training, and a long learning curve. Therefore, the interpretation of the results must be more careful.

In conclusion, our study demonstrated that LRC is superior to ORC in perioperative outcomes including EBL, blood transfusion rate, and analgesic requirement. We found no major difference in oncologic outcomes. However, the number of patients is too small to allow for a final conclusion. Future large sample-size RCTs with longer follow-up are needed to provided more convincing survival outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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