

ORIGINAL ARTICLE

Laparoscopic limited liver resection decreases morbidity irrespective of the hepatic segment resected

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Abstract

Objectives: The laparoscopic approach is widely used in abdominal surgery. However, the benefits of laparoscopy in liver surgery have hitherto been insufficiently established. This study sought to investigate these benefits and, in particular, to establish whether or not the laparoscopic approach is beneficial in patients with lesions involving the posterosuperior segments of the liver.

Methods: Outcomes in a cohort of patients undergoing mostly minor hepatectomy (50 laparoscopic and 52 open surgery procedures) between January 2000 and December 2010 at the University Clinic of Navarra were analysed. The two groups displayed similar clinical characteristics.

Results: Patients submitted to laparoscopic liver resection (LLR) had a lower risk for complications [odds ratio (OR) = 0.24, 95% confidence interval (CI) 0.07–0.74; $P = 0.013$] and shorter hospital stay (OR = 0.08, 95% CI 0.02–0.27; $P < 0.001$) independently of the presence of classical risk factors for complications. In the cohort of patients with lesions involving posterosuperior liver segments (20 laparoscopic, 21 open procedures), LLR was associated with significantly fewer complications (OR = 0.16, 95% CI 0.04–0.71) and a lower risk for a long hospital stay (OR = 0.1, 95% CI 0.02–0.43).

Conclusions: This study confirms that the laparoscopic approach to hepatic resection decreases the risk for post-surgical complications and lengthy hospitalization in patients undergoing minor liver resections. This beneficial effect is observed even in patients with lesions located in segments that require technically difficult resections.

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Introduction

The laparoscopic approach has emerged as the operative choice in many abdominal conditions. The diffusion of laparoscopy in liver surgery has been slow because the surgical technique is complex and requires surgeons to be expert in both laparoscopy and hepatic resection. Different single-centre series and a recent review¹ have shown that laparoscopic liver resection (LLR) is feasible and safe. However, the possible advantages of LLR over open liver resection (OLR) require deeper study as the benefits of the laparoscopic approach in this type of surgery are not as clear as those in the treatment of other abdominal pathologies. Most

published papers^{2–4} that report studies of this type of surgery are based on small series. Although a meta-analysis⁵ including 32 articles seems to confirm the superiority of LLR over OLR, larger series are needed to confirm this.

By contrast, most of the reported series of LLR include peripheral lesions located in the anteroinferior segments (II, III, IVb, V and VI) and there are no comparative studies assessing the possible benefits of LLR over OLR in lesions located in the posterosuperior segments (VII, VIII and IVa). It is unknown whether LLR is safer than OLR in procedures carried out in patients with lesions located in segments that imply technically more difficult resections.

The aim of this study was to compare the outcomes of LLR with those of OLR, particularly in terms of morbidity, taking into account the effects of possible confounding factors. Additional interest was paid to patients with lesions affecting unfavourable segments in order to gain better insight into the role of LLR in these technically difficult resections.

Materials and methods

Patient characteristics

A total of 445 hepatectomies were performed at the University Clinic of Navarra Department of General Surgery between January 2000 and December 2010. Of these, 392 were performed using an open approach and 53 were carried out laparoscopically. All were performed by the same surgical team. Indications for LLR were not consistent over time as this period included a learning curve. As experience accrued, indications for LLR were expanded.

A sample of 53 patients submitted to open partial hepatectomies that were similar in nature to those performed in the LLR group were selected. Selection parameters referred to the level of technical difficulty of the surgery in terms of the location, diameter and nature of the lesion(s), presence of cirrhosis, previous supramesocolic surgery, and type of liver resection. Three patients in the LLR group and one in the OLR group were excluded because they had been included in the study for a previous liver resection. Therefore, 102 patients who underwent partial hepatectomy were included in the study; these included 50 patients in the LLR group and 52 in the OLR group. A subgroup analysis of patients treated for a lesion located in the posterosuperior liver segments (20 in the LLR group and 21 in the OLR group) was performed.

Outcome measures

The main outcome was complication rate, classified according to Clavien–Dindo scores.^{6,7} Complications were defined as including both surgical and medical complications.

The amount of intraoperative blood loss was estimated indirectly by subtracting the first postoperative haemoglobin (Hb) level (measured in a blood sample taken at 12–20 h after surgery) from the preoperative level (measured in a blood sample taken in the week before the intervention).⁸ A decrease in Hb level of ≥ 2 g/dL was considered significant for this analysis. The rate of red blood cell transfusion was recorded. The hospital length of stay (LoS) was analysed; a stay of ≥ 5 days was considered relevant and was thus studied specifically. Negative (R0) resection margins were also analysed.

Patients who were converted from laparoscopic to open resection were analysed by intention to treat.

Surgical procedure

Laparoscopic liver resections

All of the laparoscopic resections were totally laparoscopic procedures. A pneumoperitoneum was established with carbon dioxide at 12 mmHg using a Veress needle, except in the first 15 patients,

in whom an open technique was used. For lesions located in segments II, III, IVa and IVb, and anterior areas of segments V and VIII, the patient was placed in the supine position with the legs apart. For lesions located in segments VI and VII, and posterior areas of segments V and VIII, the patient was placed in the left lateral position (Fig. 1a–e). Left lateral sectorectomies were performed according to the technique described by other authors⁹ and left hepatectomies were carried out using an extra-Glissonian approach as described elsewhere.¹⁰ An endo-ultrasound examination using a 5–9-MHz laparoscopic transducer (Philips HDI 5000; Philips Medical Systems, Inc., Bothell, WA, USA) was initially performed to confirm the extent of liver disease and define the surgical margins on the liver surface in all patients. Margins were typically of 1 cm (if the anatomy was amenable). Additionally, ultrasound-guided parenchymal transection was performed to monitor the lateral and deep surgical margins. Any Pringle's manoeuvre applied was performed according to the extracorporeal method previously described.¹¹ Major portal and hepatic veins were controlled with endoclips or endoscopic stapling devices. Parenchymal transection was accomplished with Ligasure V® (Valleylab, Inc., Boulder, CO, USA). When transection was completed, haemostasis was secured using bipolar forceps and occasionally with the monopolar radiofrequency coagulator TissueLink® (Salient Surgical Technologies, Inc., Portsmouth, NH, USA). The specimen was placed in a bag and removed through a suprapubic incision. In patients undergoing limited resection, and therefore the removal of a small specimen, the specimen was removed through an enlarged trocar incision. No suction drain was left in the hepatic surgical bed in any patient. Occasionally a drain was left when an additional gastric or colorectal surgery was performed.

Open liver resections

Open resections were performed using a right subcostal incision with or without an upward midline extension and in some patients through a J-shaped laparotomy. In all patients, intraoperative ultrasound was used to facilitate the marking of a transection line and to exclude previously undetected lesions. In most patients, the Cavitron ultrasonic surgical aspirator (CUSA; Valleylab, Inc.) and a TissueLink® device for liver transection were used. Intraparenchymal control of the major vessels was obtained with non-absorbable sutures or clips. In some instances, endovascular staplers were used to transect major vascular pedicles. In most of the resections, the parenchymal transection line was covered with a biological fibrin sealant (Tissucol®; Baxter AG, Vienna, Austria) or using fleece-bound sealing (Tachosil®; Takeda Pharmaceuticals International GmbH, Zurich, Switzerland). In the first 26 patients (50%), a drain was left next to the dissected liver.

Statistical analysis

Continuous variables, expressed as the mean \pm standard deviation or median [interquartile range (IQR)], were compared using the Mann–Whitney *U*-test. Categorical variables were compared

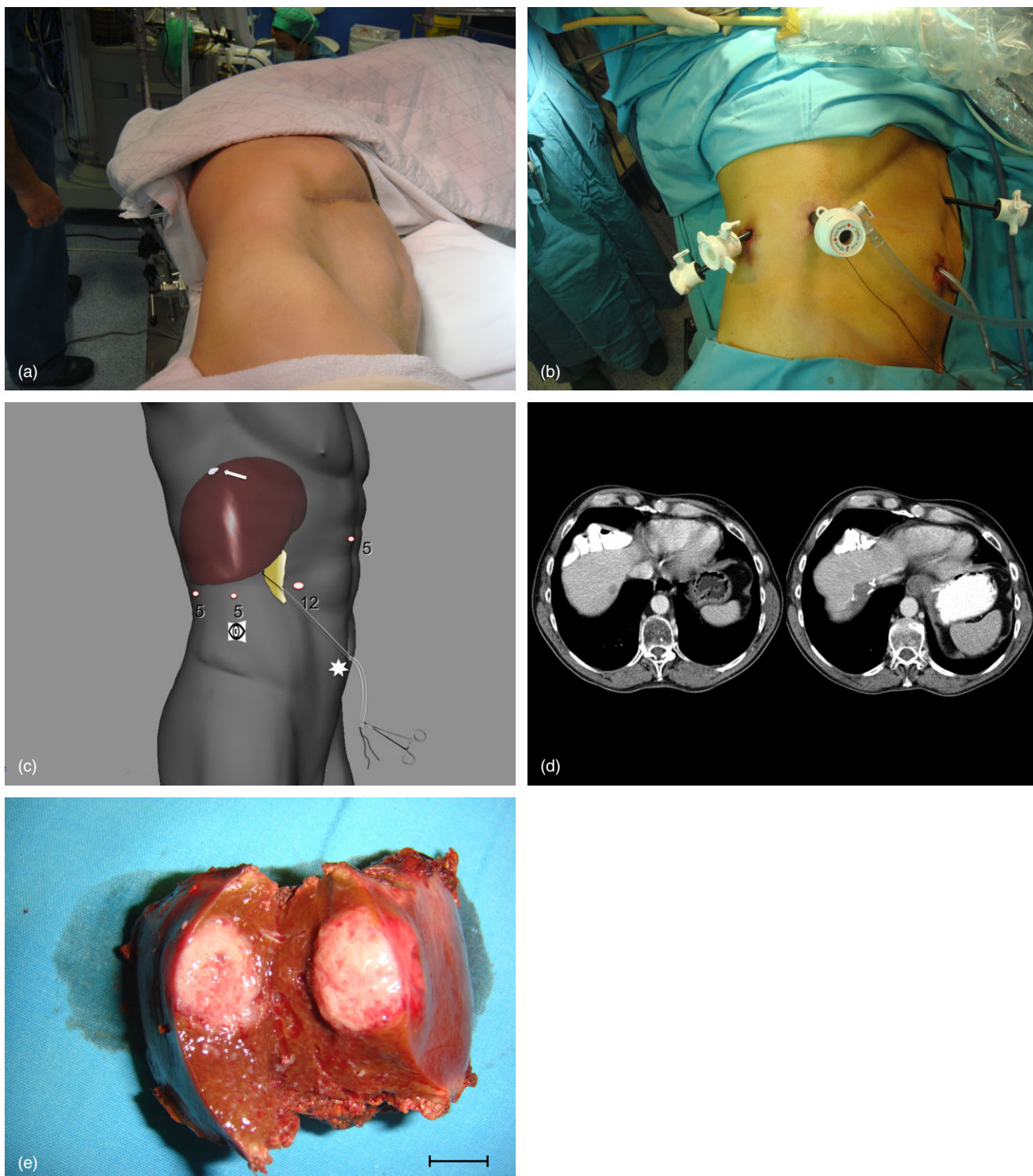


Figure 1 Resection of a solitary metastasis in the upper part of segment VII. (a) The patient is placed in the left lateral position. (b) A trocar is placed with an extracorporeal tourniquet.¹¹ (c) Schema of the patient and trocar position: the white arrow points to the lesion; the asterisk indicates the point at which the tourniquet becomes extracorporeal; the eye shows the optical trocar (a 5-mm camera was used). Numbers indicate dimensions in mm. (d) Computed tomography images pre- and post-resection. (e) The specimen

using the chi-squared or Fisher's exact tests, as appropriate. Binary logistic regression analysis was used to evaluate the risk for complications and a long LoS associated with LLR. Univariate and multivariate analyses were performed, adjusting for age, gender, use of the Pringle manoeuvre and use of a drain. Interaction (effect modification) was assessed introducing product-terms in the regression models and considering any *P*-value of <0.05 for the likelihood ratio test of this product-term as evidence of a significant interaction. Statistical analyses were performed using SPSS Version 15.0 (SPSS, Inc., Chicago, IL, USA).

Results

The two groups of patients were well matched in terms of their main demographic characteristics, clinical characteristics of their disease and the type of surgery conducted (Table 1). All patients with cirrhosis were of Child–Pugh class A status, except one patient in the LLR group with cirrhosis of Child–Pugh class B. Use of the Pringle manoeuvre and drains was more frequent among OLR patients (Table 1).

Median operating time was significantly longer in LLR patients than in those undergoing OLR [240 min (IQR: 210–313 min) versus 218 min (IQR: 183–260 min); *P* = 0.001]. Laparoscopic resections were converted to open procedures in two (4%) patients because of intraoperative bleeding. In both patients, the lesions were peripheral (segments VI and V, respectively). The causes of conversion were portal vein branch bleeding in the first patient and pelvic venous bleeding in the second patient, in whom a synchronous sigmoid resection was performed. This second patient, a cardiac transplant recipient with American Society of Anesthesiologists (ASA) class 4 status, ultimately developed multi-organ failure and died.

Analysis of overall complications

The risk for any complication was significantly lower in LLR patients. After adjusting for age, gender, Pringle manoeuvre and use of a drain, this risk remained unaltered, which suggests that the laparoscopic approach is an important independent protective factor against complications (Table 2). Moreover, postoperative complications were not only less frequent in LLR patients, but were also less severe (Table 3). The beneficial effect of LLR was retained in univariate analysis restricted to surgical complications (19 events), but not in that restricted to medical complications (Table 2). No significant multiplicative interaction between laparoscopic approach and age, gender, use of a Pringle manoeuvre or use of a drain was observed. Finally, reoperation rates were 2% in the LLR group and 6% in the OLR group, although this difference was not statistically significant (*P* = 0.616).

Bleeding and transfusion

The median decrease in Hb was significantly greater in the OLR group [2.15 g/dL (IQR: 1.3–3.1 g/dL) versus 1.5 g/dL (IQR: 0.8–

Table 1 Clinical characteristics of patients undergoing laparoscopic and open hepatectomy

	OLR group (<i>n</i> = 52)	LLR group (<i>n</i> = 50)	<i>P</i> -value
Age, years, median (IQR)	61 (52–68)	61 (48–69)	0.913
Sex, female, <i>n</i> (%)	19 (36%)	18 (35%)	0.955
BMI, kg/m ² , mean ± SD	26.1 ± 3.7	26.1 ± 4.6	0.917
ASA class, median (IQR)	3 (2–3)	3 (2–3)	0.768
Location of the lesion ^a , <i>n</i> (%)			0.962
Anteroinferior	31 (59%)	30 (60%)	
Posterosuperior	21 (40%)	20 (40%)	
Lesion diameter ^a , mm, median (IQR)	30 (23–46)	26 (15–40)	0.206
Nature of the lesion, <i>n</i> (%)			0.928
Benign	6 (11%)	8 (16%)	
Hepatocarcinoma	15 (29%)	13 (26%)	
Colorectal metastasis	21 (40%)	19 (38%)	
Other malignancies	10 (19%)	10 (20%)	
Multiple lesions, <i>n</i> (%)	4 (8%)	4 (8%)	0.951
Cirrhosis, <i>n</i> (%)	9 (17%)	10 (20%)	0.723
Previous supramesocolic surgery, <i>n</i> (%)	10 (19%)	8 (16%)	0.665
Type of liver resection, <i>n</i> (%)			0.829
Atypical or segmentectomy	42 (81%)	38 (76%)	
Sectionectomy	8 (15%)	10 (20%)	
Hemi-hepatectomy	2 (4%)	2 (4%)	
Additional surgery, <i>n</i> (%)	8 (15%)	10 (20%)	0.546
Pringle manoeuvre ^b			
Rate, <i>n</i> (%)	42 (89%)	29 (58%)	<0.001
Time, min, median (IQR)	45 (25–66)	39 (25–56)	0.667
Drain, <i>n</i> (%)	26 (50%)	5 (10%)	<0.001

^aIn cases of multiple lesions, the most unfavourable lesion was considered.

^bInformation for five patients in the OLR group is lacking.

OLR, open liver resection; LLR, laparoscopic liver resection; IQR, interquartile range; BMI, body mass index; SD, standard deviation; ASA, American Society of Anesthesiologists.

2.3 g/dL); *P* = 0.007]. Rates of transfusion were 23% in patients undergoing OLR and 12% in patients undergoing LLR (*P* = 0.146).

The risk for a preoperative versus a postoperative Hb reduction of ≥2 g/dL was clearly decreased in LLR (Table 2). When a multivariate analysis including age, gender, use of a Pringle manoeuvre and use of a drain was performed, the protective effect of laparoscopy on the decrease in Hb remained evident, although the significance was lost (Table 2). In this analysis, no significant interaction between LLR and age, gender, use of a Pringle manoeuvre and use of a drain was observed.

Hospital LoS

The median hospital LoS was significantly shorter after LLR than after OLR [4 days (IQR: 3–5 days) versus 7 days (IQR: 6–9 days);

Table 2 Univariate and multivariate analyses of complications, bleeding and length of stay associated with laparoscopic hepatectomy

Variable	OLR group (n = 52)	LLR group (n = 50)	Univariate OR (95% CI)	P-value	Multivariate OR ^a (95% CI)	P-value
Total complications, n (%)	24 (46%)	8 (16%)	0.22 (0.08–0.56)	0.002	0.24 (0.07–0.74)	0.013
Surgical	14 (27%)	5 (10%)		0.044		
Medical	14 (27%)	7 (14%)		0.141		
Hb decrease of ≥2 g/dL, n (%)	26 (52%)	14 (30%)	0.4 (0.17–0.93)	0.034	0.38 (0.13–1.09)	0.072
Length of stay of ≥5 days, n (%)	41 (79%)	10 (20%)	0.07 (0.02–0.19)	<0.001	0.08 (0.02–0.27)	<0.001

^aModel adjusted for age, gender, Pringle manoeuvre and use of drain.

OLR, open liver resection; LLR, laparoscopic liver resection; OR, odds ratio; 95% CI, 95% confidence interval; Hb, haemoglobin.

Table 3 Severity of complications, according to Clavien–Dindo score, following liver resection

	OLR group (n = 52)	LLR group (n = 50)	P-value
Clavien–Dindo class 1/2/3/ 4/5, n	6/6/6/6/0	1/3/1/2/1	0.016
Clavien–Dindo class ≥2, n (%)	18 (35%)	7 (14%)	0.016
Clavien–Dindo class 5 (mortality), n (%)	0	1 (2%)	0.999

OLR, open liver resection; LLR, laparoscopic liver resection.

Table 4 Resection margins in patients operated for malignant lesions

	OLR group (n = 43)	LLR group (n = 42)	P-value
Resection margins, mm, median (IQR)	10 (3–10)	10 (6–15)	0.007
Resection margins, n			0.121
≥1 cm	22	28	
<1 cm	18	14	
Positive margin	3	0	

OLR, open liver resection; LLR, laparoscopic liver resection; IQR, interquartile range.

($P = 0.001$)). The laparoscopic technique was associated with a substantial drop in the risk for a prolonged hospital stay (≥5 days). Again, no significant interaction between the use of the laparoscopic approach and age, gender, Pringle manoeuvre or use of a drain was detected (Table 2).

Pathologic results

As Table 4 shows, surgical margins were similar in both groups of patients.

Complications in patients with lesions in the posterosuperior segments

A total of 41 patients (21 in the OLR group and 20 in the LLR group) were treated for lesions located in a posterosuperior liver

segment. The demographic and clinical characteristics of patients in both groups, as well as the characteristics of the lesions, were similar (data not shown) and thus the two groups were comparable. As Table 5 shows, patients in this category also clearly benefited from the minimally invasive approach in terms of complication rate, Hb decrease and LoS. Among those patients with malignant lesions (20 in the LLR group and 17 in the OLR group), LLR patients showed wider surgical margins [median = 10 mm (IQR: 6–14 mm)] than OLR patients [median = 7 mm (IQR: 4–10 mm)] ($P = 0.021$).

Discussion

This study shows further evidence of the advantages of minimally invasive liver surgery over open liver surgery in terms of morbidity and LoS. The lower incidence of complications in laparoscopic hepatectomies was described by Rao *et al.* in 2012 in a meta-analysis that included the 32 most relevant comparative studies published to date.⁵ However, single-institution studies comparing open and laparoscopic approaches are limited. To the present authors' knowledge, only four studies have investigated outcomes in equivalent numbers of patients operated by totally laparoscopic surgery^{12–15} and all of these report results similar to those presented here. Beyond these similarities in findings, the present study makes an important original contribution by noting that the reduction in the complication rate associated with the laparoscopic approach is independent of the demographic and clinical characteristics of the patients, as well as of the characteristics of the tumour. Another aspect that has not yet been adequately studied is the degree of severity of complications in these patients.^{14,16,17} This study suggests that the severity of complications is lower in patients operated laparoscopically. This undoubtedly would underline the clinical benefit of this surgical approach in liver surgery. Nonetheless, it should be noted that almost 75% of the patients included in the present study underwent segmentectomies or limited resections.

Bleeding is among the most dreaded of intraoperative incidents during liver surgery and its reduction can have an important clinical impact. Although actual intraoperative bleeding was not measured directly in the present study, some conclusions can be drawn from the rate of transfusion and the decrease in Hb levels

Table 5 Analysis of complications, bleeding and length of stay associated with laparoscopic hepatectomy of posterosuperior segments

Variable	OLR group (n = 21)	LLR group (n = 20)	Univariate OR (95% CI)	P-value
Total complications, n	11	3	0.16 (0.04–0.71)	0.017
Hb decrease of ≥ 2 g/dL, n	14	6	0.23 (0.06–0.86)	0.033
Length of stay of ≥ 5 days, n	17	6	0.10 (0.02–0.43)	0.002

OLR, open liver resection; LLR, laparoscopic liver resection; OR, odds ratio; 95% CI, 95% confidence interval; Hb, haemoglobin.

during surgery. These results suggest a possible association between LLR and a reduction in blood loss, which is consistent with the results of previous studies.^{2,4,16,18–22} One important consequence of this finding is that it will incur a trend towards a reduced need for transfusions among this group of patients, thus saving health resources and decreasing the risks associated with transfusion.

One of the great advantages of laparoscopy, which is not exclusive to liver surgery, is its affordance of a significant reduction in hospital stay. Almost all publications on LLR report a significant reduction in hospital stay.^{14,16,23–25} The present study shows a similar finding, but suggests that this beneficial effect of LLR is independent of the patients' clinical characteristics.

One controversial issue in the literature concerns how lesions located in the posterosuperior segments should be approached.^{1,26–29} These segments have been considered more difficult to operate on using a laparoscopic approach because visualization is limited and it is difficult to control bleeding.³⁰ Theoretically, these factors may raise the risk for intra- and postoperative complications. This is why some authors contraindicate LLR in these patients and propose instead an open approach or, in selected patients, hand-assisted LLR.^{1,13,31–34} Although some small series of LLR of the posterosuperior segments have been published,^{30,35–37} the present study is, to its authors' knowledge, the first to directly compare both open and laparoscopic approaches to the resection of these lesions and it contributes towards resolving the controversy on whether or not these resections are feasible and safe. Importantly, this study suggests that, despite its technical difficulty, there are benefits to be derived from the use of totally laparoscopic surgery in these patients.

The present study has some limitations. It is a non-randomized retrospective study. No randomized study has been published to date and thus, until one is available, all additional partial evidence is useful. This study may also have been subject to selection bias. As stated in the Materials and methods section, selection criteria for LLR were expanded over time. Thus, patients who underwent open procedures were operated on slightly earlier than patients in the LLR group. This bias was minimized by the choice of a period of study in which the technique for the open approach was kept unaltered. In addition, the patients in the OLR group were carefully selected to match those in the LLR group in terms of the locations, diameters and nature of their lesions.

In summary, the present study strongly suggests that patients undergoing LLR may have fewer (and less severe) surgical com-

plications and shorter postoperative hospital stays than those treated using an open approach. It also suggests that these benefit of the laparoscopic approach are independent of other risk factors. Importantly, patients with lesions located in the posterosuperior segments also benefit from a totally laparoscopic approach in terms of complication rates and LoS.

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Conflicts of interest

None declared.

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