Original article

Risk factors and consequences of conversion in laparoscopic major liver resection

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Background: **Although recent reports have suggested potential benefits of the laparoscopic approach in patients requiring major hepatectomy, it remains unclear whether conversion to open surgery could offset these advantages. This study aimed to determine the risk factors for and postoperative consequences of conversion in patients undergoing laparoscopic major hepatectomy (LMH).**

Methods: **Data for all patients undergoing LMH between 2000 and 2013 at two tertiary referral centres were reviewed retrospectively. Risk factors for conversion were determined using multivariable analysis. After propensity score matching, the outcomes of patients who underwent conversion were compared with those of matched patients undergoing laparoscopic hepatectomy who did not have conversion, operated on at the same centres, and also with matched patients operated on at another tertiary centre during the same period by an open laparotomy approach.**

Results: **Conversion was needed in 30 (13·5 per cent) of the 223 patients undergoing LMH. The most frequent reasons for conversion were bleeding and failure to progress, in 14 (47 per cent) and nine (30 per cent) patients respectively. On multivariable analysis, risk factors for conversion were patient age above 75 years (hazard ratio (HR) 7·72, 95 per cent c.i. 1·67 to 35·70; *P* = 0·009), diabetes (HR 4·51, 1·16 to 17·57; *P* = 0·030), body mass index (BMI) above 28 kg/m^2 (HR 6·41, 1·56 to 26·37; *P* = 0·010), tumour diameter greater than 10 cm (HR 8·91, 1·57 to 50·79; *P* = 0·014) and biliary reconstruction (HR 13·99, 1·82 to 238·13; *P* = 0·048). After propensity score matching, the complication rate in patients who had conversion was higher than in patients who did not (75 *versus* 47·3 per cent respectively; *P* = 0·038), but was not significantly different from the rate in patients treated by planned laparotomy (79 *versus* 67·9 per cent respectively; *P* = 0·438).**

Conclusion: **Conversion during LMH should be anticipated in patients with raised BMI, large lesions and biliary reconstruction. Conversion does not lead to increased morbidity compared with planned laparotomy.**

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Introduction

Since the first report of a successful laparoscopic liver resection (LLR), diffusion of the laparoscopic approach in liver surgery has been slow because of initial concerns regarding operative risks, oncological issues[1,2] and technical difficulties. Nevertheless, laparoscopy has now been shown to provide several advantages over laparotomy, including diminished blood loss[3], fewer complications[4–7] and ascites[5,6,8], as well as shorter hospital stays[9,10]. These benefits are thought to be related to the pneumoperitoneum, which limits blood loss and may enhance inflow occlusion when prior selective vascular inflow control is performed, but are also related to the absence of a large incision. The smaller incisions allow preservation of collateral abdominal wall vascularization in patients with cirrhosis, diminish postoperative pain and enhance early rehabilitation. In this setting, although conversion to open liver resection would intuitively offset these benefits, its true influence on the postoperative course of patients undergoing LLR is still unanswered.

Laparoscopic major hepatectomy (LMH) is currently considered the most challenging LLR procedure. It requires mastery of both laparoscopic pedicular dissection and parenchymal transection of large-sized cut surfaces. Hence it is generally accepted that LMH should be attempted only after considerable expertise in LLR has been acquired[11]. Still, even in experienced hands, approximately 10–20 per cent of patients undergoing major LLR require conversion to open hepatectomy[12–15], whereas standard LLR is associated with conversion rates of less than 5 per cent[16]. LMH could represent a relevant model for accurate identification of preoperative risk factors for, and consequences of, conversion in order to improve the perioperative management of these patients.

The present study aimed to determine the risk factors for conversion to open hepatectomy and to analyse the postoperative consequences of conversion in patients undergoing LMH using propensity score matching of patients operated on at three tertiary-referral hepatopancreatobiliary units.

Methods

The study included all patients undergoing fully laparoscopic major (at least 3 contiguous Couinaud segments[17]) right or left liver resection at the Institut Mutualiste Montsouris (centre 1) in 2000–2013 and at Hôpital Saint Antoine (centre 2) in 2009–2013, as well as all patients undergoing open major hepatectomy at Hôpital Beaujon (centre 3) in 2000–2013. No patient had a planned hand-assisted or hybrid approach. For centre 2, the first major LLRs were performed in 2007, but relocation of the surgical team to another hospital in 2009 prevented collection of data before 2009. In centre 3 no patient underwent LMH during the study interval. The collected data were retrieved from prospectively maintained databases and included baseline patient characteristics such as demographic data, preoperative risk factors and co-morbidities, type of preoperative management, operative characteristics including intraoperative incidents, pathological data and postoperative outcomes. The study was approved by the local institutional review board at each centre.

Surgical technique

Laparoscopy group

All procedures were performed by at least one senior surgeon. Liver transection was done under low (less than 5 mmHg) central venous pressure[18]. Briefly, LMH was performed using five or six ports depending on the surgical procedure and operator preference, as described previously[12,19]. Laparoscopic ultrasonography was used routinely to guide the resection. The operative technique was similar to that for open surgery: isolation and division of hepatic inflow, absence of mobilization of the liver before transection, and subsequent transection of liver parenchyma. Clamping of the hepatic inflow pedicle was not performed routinely during this step, and the Pringle manoeuvre was used only when there was bleeding. Energy sources and parenchymal division techniques varied throughout the study period. During the early years, tissue dissection and haemostasis were performed using ultrasonic dissector or scalpel, while bipolar forceps provided retraction and haemostasis. In more recent years, the harmonic scalpel (primarily SonoSurg®; Olympus, Tokyo, Japan) and, more recently, Harmonic® (Ethicon EndoSurgery, Cincinnati, Ohio, USA) or Thunderbeat® (Olympus, Tokyo, Japan) was frequently used, especially for transection of superficial parenchyma. When parenchymal transection reached the hilar plate, segment I was divided along the right aspect of the inferior vena cava. This step is essential to allow dissection of both the right bile duct and the hilar plate, which were then taped, closed using either a large secured clip or a stapler, and finally cut. At the end of parenchymal transection, the hepatic outflow was divided with an endoscopic vascular stapler. The resected specimen was finally mobilized, placed in a plastic bag and removed, without fragmentation, preferentially through a 5–8-cm suprapubic incision without muscle section. This incision was closed immediately and the abdomen reinsufflated to confirm haemostasis and absence of bile leaks. Methylene blue or air injection through the cystic drain was not performed routinely. Abdominal drainage was used only when there was concern about intraoperative bile control or the adequacy of haemostasis, regardless of the approach.

Selection criteria for the use of the laparoscopic approach evolved over time and varied according to centre, but patients qualified for LMH only when lesions were far from the liver hilum, hepatocaval junction and inferior vena cava. All lesions had to be well clear of the mid-plane of the liver to allow adequate surgical margins. Hence, laparoscopy was contraindicated when total vascular exclusion without or with liver cooling and reconstruction of major vascular structures (portal vein/branch or hepatic vein/inferior vena cava) were required. Although the laparoscopic approach was avoided initially in patients with huge lesions and those requiring biliary reconstruction, these situations did not represent absolute contraindications to the laparoscopic approach in more recent years. Previous abdominal surgery, obesity, underlying cirrhosis, bilobar disease and previous portal vein embolization were not considered contraindications to the laparoscopic approach.

Conversion to open surgery

Conversion was defined as the requirement for laparotomy at any time of the procedure, except extraction of the resected specimen. For the purpose of this study, specific data regarding conversion were retrieved from the operative reports. These included reasons for conversion, and the timing and type of conversion. Reasons for conversion were categorized as: haemorrhage considered difficult to control under laparoscopy, failure to progress, existence of tight adhesions, operative discovery of unexpected tumour spread and operative incident (excluding haemorrhage). Timing of conversion was defined as follows: before pedicular dissection; between pedicular dissection and hilar plate section; and from hilar plate section to the end of the procedure. The types of conversion were categorized as: subcostal incision, J-shaped incision, midline incision and hand port placement. Finally, conversion rates were compared according to the experience of each centre. In this setting, early experience and late experience accounted for the first half and second half respectively of the total number of patients operated on.

Planned laparotomy group

At centre 3, all procedures were performed by at least one senior surgeon. The procedures were carried out through bilateral or J-shaped incision depending on tumour location and surgeon preference. Liver transection was performed under low central venous pressure[18] without prior mobilization, using the hanging manoeuvre in most patients and the crush-clamp technique or ultrasonic dissection, as described[20]. Haemostasis and control of bile leaks was achieved by means of bipolar cautery coagulation, or ligation for small pedicles. Intermittent pedicle clamping was performed in the event of bleeding, or in some patients to obtain a bloodless operative field. Methylene blue injection through the cystic drain was performed selectively to rule out biliary leakage.

Postoperative data

After surgery, all patients were seen daily by a physician until hospital discharge. Liver function tests were performed on postoperative day (POD) 1, 3, 5, 7 and 10. Chest radiography was carried out routinely on POD 1 and 3 in all centres. Thoracoabdominopelvic CT with intravenous contrast injection was performed selectively in patients with suspected abdominal or thoracic complications. Specific liver-related complications were categorized as follows: liver failure was defined according to the '50–50 criteria' on POD 5[21]; ascites was defined as abdominal drainage output of more than 10 ml per kg per day after POD 3[22]; haemorrhage was defined as a reduction in haemoglobin level of more than 3 g/dl after the end of surgery, compared with postoperative baseline level, and/or any postoperative transfusion of packed red blood cell units for a falling haemoglobin concentration, and/or the need for invasive reintervention[23]; finally, biliary leakage was defined by a bilirubin concentration in the drainage fluid more than threefold that in serum[24]. Liver parenchyma was assessed according to the presence of both fibrosis and steatosis. Fibrosis score ranged from 0 to 4[25] and was considered severe in patients with stage F3 and F4, whereas steatosis was considered significant when above 30 per cent. Postoperative complications were stratified according to the Dindo–Clavien classification[26], which defines major complications by a score of III or more. Complications and operative mortality were considered as those occurring within 90 days of surgery, or at any time during the postoperative hospital stay.

Study design

Risk factors for conversion and postoperative complications were analysed. The influence of conversion on the postoperative course of patients undergoing LMH was then assessed by comparing the postoperative course of patients who had conversion with that of patients who did not, before and after propensity score adjustment for the risk factors for conversion. Using this propensity score matching method, the two groups would be similar in terms of preoperative characteristics along with risk factors for postoperative complications, thus allowing the effect of conversion on the postoperative course of the patients to be analysed. Finally, to determine whether conversion led to a more impaired postoperative course than planned laparotomy, the postoperative outcomes of patients who had conversion were compared with those of matched controls undergoing major liver resection at centre 3 during the same period, before and after propensity score adjustment on factors known to influence the type of approach (laparoscopy or laparotomy).

Statistical analysis

Quantitative variables are expressed as mean or median (range) as appropriate. Qualitative variables are expressed as frequencies. Mann–Whitney U test was used for intergroup comparisons of quantitative variables as appropriate, whereas the χ^2 test or Fisher's exact test was used to compare categorical data. Probabilities of undergoing conversion and experiencing postoperative complications were estimated using a multivariable logistic regression model. All variables that differed significantly in

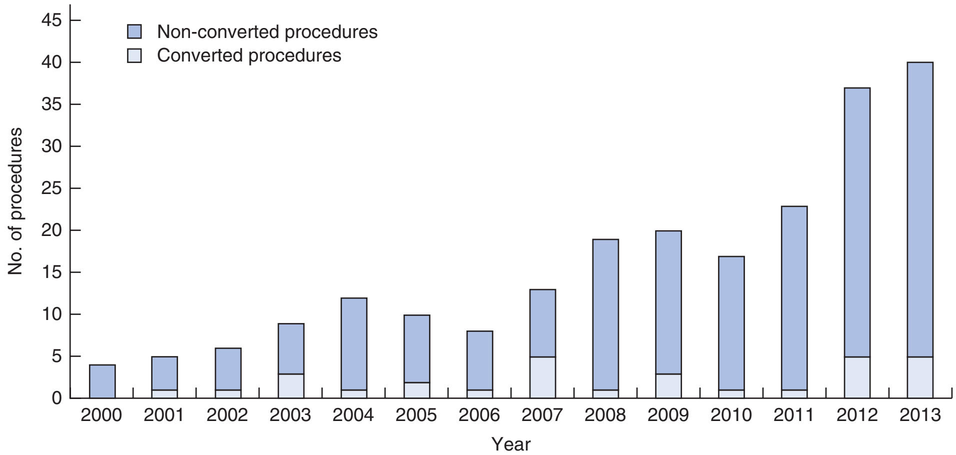

Fig. 1 Resections and conversions in patients undergoing major laparoscopic hepatectomy according to year, 2000–2013

univariable analysis ($P<0{\cdot}100$), when comparing the two groups, were included in the logistic model and backward selection was applied. For propensity score analysis, the logistic regression model was based on the assessment of goodness-of-fit statistics proposed by Lemeshow and Hosmer[27]. In this setting, for comparison of postoperative complication rates between patients who did, or did not have a conversion, propensity score adjustment was performed on the factors that were significantly associated with conversion on multivariable analysis. Similarly, for comparison of postoperative complication rates between patients who had a conversion and those who had open surgery, propensity score adjustment was performed on the factors known to influence the choice of approach. The latter included baseline characteristics (sex, age, American Society of Anesthesiologists (ASA) fitness grade, body mass index (BMI)), co-morbidities (diabetes, chronic obstructive pulmonary disease (COPD), ischaemic heart disease), presence of severe underlying fibrosis, indication for hepatectomy (malignant/benign disease, living donation), tumour characteristics (number, size), type of resection (right, left, extended right, extended left) and extent of resection (biliary and vascular reconstruction, associated hepatic and extrahepatic resection). Using these propensity scores, patients who had a conversion were randomly matched to patients who did not, and to patients who had planned open surgery using 1 : 7 and 1 : 10 interval matching methods respectively. Thereafter, the groups were compared to examine the balance between variables and whether there were statistical differences in baseline variables between the groups. Finally, after assuring the comparability of the groups, comparison of postoperative complication rates between the groups was performed using χ^2 or Fisher's exact test as appropriate. All statistical analyses were performed with SPSS® version 20.0 (IBM, Armonk, New York, USA).

Table 1 Timing of conversion according to the reason for conversion and type of conversion

	Before pedicular dissection (*n* = 5)	Between pedicular dissection and hilar plate section (*n* = 7)	After hilar plate section (*n* = 18)
Reason for conversion			
Bleeding	0 (0)	1 (14)	13 (72)
Failure to progress	0 (0)	6 (86)	3 (17)
Adhesions	3 (60)	0 (0)	0 (0)
Operative incident	0 (0)	0 (0)	2 (11)
Need for further exploration	2 (40)	0 (0)	0 (0)
Type of conversion			
Subcostal incision	2 (40)	2 (29)	14 (78)
J-shaped incision	2 (40)	4 (57)	0 (0)
Midline incision	1 (20)	1 (14)	2 (11)
Hand-assisted	0 (0)	0 (0)	2 (11)

Values in parentheses are percentages.

Results

A total of 223 patients underwent LMH during the study period; there were 135 men (60·5 per cent) and 88 women (39·5 per cent). Median age was 63·5 (23·9–86·2) years, and 35 patients (15·7 per cent) were aged over 75 years. Median BMI was 24·9 (15·9–35·5) kg/m^2; 54 patients (24·2 per cent) had a BMI above 28 kg/m^2. Indications for liver resection were malignant disease in 197 patients (88·3 per cent), including colorectal liver metastases in 112 (50·2 per cent, hepatocellular carcinoma in 44 (19·7 per cent), cholangiocarcinoma in 27 (12·1 per cent) and other types of malignancy in 14 (6·3 per cent). Before liver resection, 87 patients (39·0 per cent) received chemotherapy, comprising more than six cycles in 63 patients (28·3 per cent). Preoperative portal vein embolization (PVE) and transarterial chemoembolization (TACE) were performed in 45 (20·2 per cent) and 13 (5·8 per cent) patients respectively. A total of 11 patients (4·9 per cent) underwent sequential TACE–PVE. Of the 26 patients (11·7 per cent) operated on for benign lesions, indications for liver resection were liver cell adenoma in six patients (2·7 per cent), symptomatic focal nodular hyperplasia and mucinous cystadenoma in five (2·2 per cent) each, living donation and intrahepatic stones in two patients (0·9 per cent) each, and other types of benign lesions in the remaining six patients (2·2 per cent).

Major right-sided resections were performed in 160 patients (71·7 per cent); 33 (14·8 per cent) had removal of more than four hepatic segments. Associated wedge resection or radiofrequency ablation in the contralateral lobe was performed in 24 (10·8 per cent) and seven (3·1 per cent) patients respectively. Biliary and portal reconstructions were performed in eight (3·6 per cent) and one (0·4 per cent) patients respectively. Extrahepatic procedures were performed in 16 patients (7·2 per cent), and included diaphragmatic resections in nine (4·0 per cent), colonic resection in three (1·3 per cent), and distal pancreatectomy, duodenal resection, right adrenal gland resection and right nephrectomy in one patient each (0·4 per cent). *Fig. S1* (supporting information) provides a flow chart for the study.

Conversion to open hepatectomy

Conversion to laparotomy was required in 30 patients (13·5 per cent); their characteristics are shown in *Table S1* (supporting information). *Fig. 1* represents the evolution in the number of patients who underwent conversion per year. The conversion rate was no different between centres 1 and 2 (12 *versus* 18·5 per cent; $P = 0{\cdot}201$). When the experience of each centre was divided in two periods of equal numbers of procedures (early *versus* late), the conversion rate remained stable over time (17 *versus* 11 per cent, $P = 0{\cdot}183$ for centre 1; 11 *versus* 20 per cent, $P = 0{\cdot}530$ for centre 2).

Table 1 summarizes the timing of conversion according to the reason for and the type of conversion. Although the most frequent reason for conversion was bleeding that was difficult to control laparoscopically, no critical situation due to massive acute bleeding from a major vascular structure was encountered. Failure to progress laparoscopically was related to the inability to expose pedicular structures correctly in four patients, difficult exposure during parenchymal transection in three patients, and inability to dissect the hepatocaval confluence because of a large lesion in two patients. Of the three patients with tight adhesions, two had previously undergone open abdominal surgery including partial gastrectomy and left colectomy, and one patient had primary intraperitoneal adhesions related to familial Mediterranean fever. Operative incidents accounted for a pleural breach and a biliary injury in one patient each, and the need for further exploration was required for unexpected tumour spread in two patients.

Table 2 details the results of univariable and multivariable analyses of risk factors for conversion. In multivariable analysis, age above 75 years, diabetes, BMI greater than 28 kg/m^2, tumour diameter above 10 cm and associated biliary reconstruction were significantly associated with an increased risk of conversion. More patients with a BMI above 28 kg/m^2 (24·8 per cent *versus* 11·3 per cent in the early period; $P = 0{\cdot}039$) and with lesions greater than 10 cm (15·5 *versus* 6·6 per cent respectively; $P = 0{\cdot}043$) were operated on during the latest period in both centres.

Postoperative outcomes

In the whole cohort, six patients (2·7 per cent) died during the postoperative period, including one in the conversion group ($P = 0{\cdot}815$). Death was related to biliary peritonitis in three patients, liver failure in two and postoperative haemorrhage in one. Overall 117 patients (52·5 per cent) had postoperative complications, which were major in 51 patients (22·9 per cent). *Table S2* (supporting information) details the results of univariable and multivariable analyses of the risk factors for postoperative complications. In univariable analysis, BMI above 28 kg/m^2, resection for cholangiocarcinoma, severe underlying fibrosis, resection of more than four hepatic segments, right-sided liver resection, associated radiofrequency ablation, conversion to laparotomy and abdominal drainage were significantly associated with increased rates of postoperative complications. In multivariable analysis, the existence of severe underlying fibrosis (hazard ratio (HR) 3·42, 95 per cent c.i. 2·55 to 5·87; $P = 0{\cdot}018$), right-sided resection (HR 1·93, 1·00 to 3·73; $P = 0{\cdot}049$), associated radiofrequency ablation (HR 4·38, 2·34 to 7·54; $P = 0{\cdot}004$) and conversion to laparotomy (HR 2·83, 1·09 to 7·30; $P = 0{\cdot}026$) remained significantly associated with an increased risk of postoperative complications.

Influence of conversion on postoperative course

Of the 30 patients who had conversion to open surgery, one (3 per cent) died after surgery and 23 (77 per cent) experienced postoperative complications,

Table 2 Univariable and multivariable analyses of risk factors for conversion to laparotomy

	No conversion (*n* = 193)	Conversion (*n* = 30)	*P*‡	Hazard ratio†	*P*#
Preoperative characteristics					
Age (years)*	61·9 (23·9–86·2)	67·2 (41·9–85·2)	0·035¶	–	–
> 75 years	26 (13·5)	9 (30·0)	0·021	7·72 (1·67, 35·70)	0·009
Sex ratio (M : F)	118 : 75	17 : 13	0·690§		
ASA fitness grade ≤ II	151 (78·2)	26 (87)	0·289		
Diabetes	20 (10·4)	9 (30)	0·003	4·51 (1·16, 17·57)	0·030
Hypertension	51 (26·4)	12 (40)	0·124		
Dyslipidaemia	36 (18·7)	3 (10)	0·246		
BMI > 28 kg/m^2	40 (20·7)	14 (47)	0·002	6·41 (1·56, 26·37)	0·010
Metabolic syndrome	11 (5·7)	4 (13)	0·120		
Cardiorespiratory co-morbidity	38 (19·7)	5 (17)	0·696		
Coronary heart disease	20 (10·4)	1 (3)	0·220		
COPD	15 (7·8)	5 (17)	0·113		
Tobacco use	52 (26·9)	11 (37)	0·271		
Previous abdominal surgery	120 (62·2)	14 (47)	0·107		
Colorectal surgery	77 (39·9)	8 (27)	0·165		
Hepatic surgery	31 (16·1)	2 (7)	0·178		
Other	12 (6·2)	4 (13)	0·242§		
Underlying liver disease					
Alcohol-related	37 (19·2)	6 (20)	0·915		
Viral infection	16 (8·3)	4 (13)	0·368		
Iron overload	4 (2·1)	0 (0)	0·426		
Severe fibrosis	30 (15·5)	4 (13)	0·754		
Steatosis > 30%	33 (17·1)	6 (20)	0·697		
Pathology					
Malignant disease	170 (88·1)	27 (90)	0·761		
HCC	37 (19·2)	7 (23)	0·623§		
Cholangiocarcinoma	21 (10·9)	6 (20)	0·223§		
Colorectal liver metastases	101 (52·3)	11 (37)	0·121§		
Other	11 (5·7)	3 (10)	0·366		
Benign disease	23 (11·9)	3 (10)	0·761		
Liver cell adenoma	6 (3·1)	0 (0)	0·328		
Focal nodular hyperplasia	5 (2·6)	0 (0)	0·373		
Mucinous cystadenoma	4 (2·1)	1 (3)	0·518		
Living donor	2 (1·0)	0 (0)	0·575§		
Other	6 (3·1)	2 (7)	0·374§		
Single lesion	99 (51·3)	19 (63)	0·219		
Tumour diameter > 10 cm	19 (9·8)	8 (27)	0·009	8·91 (1·57, 50·79)	0·014
Preoperative management					
Chemotherapy	80 (41·5)	7 (23)	0·071§	0·74 (0·18, 5·67)	0·321
> 6 cycles	57 (29·5)	6 (20)	0·281		
TACE	11 (5·7)	2 (7)	0·689§		
PVE	39 (20·2)	6 (20)	0·979		
Intraoperative characteristics					
> 4 resected segments	26 (13·5)	7 (23)	0·169§		
Right-sided hepatectomy	140 (72·5)	20 (67)	0·506		
Associated RFA	6 (3·1)	1 (3)	0·948		
Associated wedge resection	21 (10·9)	3 (10)	0·885		
Biliary reconstruction	4 (2·1)	4 (13)	0·013§	13·99 (1·82, 238·13)	0·048
Vascular reconstruction	0 (0)	1 (3)	0·135§		
Extrahepatic procedure	13 (6·7)	3 (10)	0·519		

Values in parentheses are percentages unless indicated otherwise; *values are mean (range) and †95 per cent c.i. in parentheses. ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; PVE, portal vein embolization; RFA, radiofrequency ablation. ‡χ^2 test, except §Fisher's exact test and ¶Mann–Whitney *U* test; #logistic regression analysis.

Table 3 Comparison of postoperative course of patients undergoing laparoscopic liver resection

	No conversion group	Conversion group	*P*‡
Overall cohort	*n* = 193	*n* = 30	
Postoperative complications	94 (48·7)	23 (77)	0·005§
Dindo–Clavien grade I–II	52 (26·9)	14 (47)	0·033§
Dindo-Clavien grade III–IV	37 (19·2)	8 (27)	0·341
Postoperative mortality	5 (2·6)	1 (3)	0·815
Ascites	12 (6·2)	4 (13)	0·242§
Liver failure	7 (3·6)	1 (3)	0·936
Abdominal collection	41 (21·2)	7 (23)	0·813§
Biliary leakage	26 (13·5)	6 (20)	0·256§
Infectious complication	41 (21·2)	8 (27)	0·485§
Respiratory complication	30 (15·5)	9 (30)	0·069§
Confusion	5 (2·6)	4 (13)	0·021§
Renal failure	6 (3·1)	4 (13)	0·032§
Haemorrhage	2 (1·0)	0 (0)	0·575
Multiple organ failure	8 (4·1)	3 (10)	0·171§
Reoperation	8 (4·1)	1 (3)	0·834§
Duration of surgery (min)*	297 (100–540)	348 (180–480)	0·017¶
Blood loss (ml)*	302 (50–1600)	623 (50–4500)	< 0·001¶
Transfusion	20 (10·4)	9 (30)	0·003
Hospital stay (days)*	10 (3–82)	12 (5–49)	0·094¶
After propensity score adjustment†	*n* = 112	*n* = 16	
Postoperative complications	53 (47·3)	12 (75)	0·038
Dindo–Clavien grade I–II	32 (28·6)	6 (38)	0·465
Dindo–Clavien grade III–IV	18 (16·1)	6 (38)	0·040
Postoperative mortality	3 (2·7)	0 (0)	0·508
Ascites	6 (5·4)	3 (19)	0·050
Liver failure	4 (3·6)	0 (0)	0·442
Abdominal collection	24 (21·4)	4 (25)	0·746
Biliary leakage	15 (13·4)	4 (25)	0·222
Infectious complication	23 (20·5)	5 (31)	0·332
Respiratory complication	15 (13·4)	3 (19)	0·564
Confusion	3 (2·7)	2 (13)	0·121§
Renal failure	4 (3·6)	2 (13)	0·114
Haemorrhage	1 (0·9)	0 (0)	0·702§
Multiple organ failure	5 (4·5)	0 (0)	0·384§
Reoperation	6 (5·4)	1 (6)	0·897§
Duration of surgery (min)*	302 (100–520)	363 (180–480)	0·032¶
Blood loss (ml)*	387 (50–1600)	616 (50–4500)	< 0·001¶
Transfusion	13 (11·6)	5 (31)	0·038
Hospital stay (days)*	10 (3–82)	13 (5–49)	0·063¶

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Propensity score adjustment was performed on the factors influencing the risk of conversion as defined by the results of multivariable analysis; these included body mass index above 28 kg/m^2, diabetes, age above 75 years and associated biliary reconstruction. ‡χ^2 test, except §Fisher's exact test and ¶Mann–Whitney *U* test.

including nine major complications (30 per cent). Neither the timing of conversion ($P = 0{\cdot}624$ for comparison between the three time periods) nor the reason for conversion ($P = 0{\cdot}749$ for comparison between the five reasons) influenced the postoperative complication rate.

Comparison of outcomes in patients who had conversion and those who did not

Table 3 details the results of the comparison of the postoperative course between patients who had a conversion and those who did not, before and after propensity score adjustment on factors associated with conversion. After propensity score adjustment, patients who underwent conversion had significantly more blood loss and transfusions than patients who did not. Likewise, the rates of overall and major postoperative complications, and postoperative ascites, were increased in the conversion group. Finally, matched patients in the conversion and no-conversion groups operated on for malignant disease had similar rates of surgical margin clearance (86 *versus* 92·9 per cent

Table 4 Postoperative course of patients who underwent conversion and patients who had planned laparotomy

	Laparotomy group	Conversion group	*P*‡
Overall cohort	*n* = 770	*n* = 30	
Postoperative complications	532 (69·1)	23 (77)	0·427§
Dindo–Clavien grade I–II	323 (41·9)	14 (47)	0·707§
Dindo–Clavien grade III–IV	172 (22·3)	8 (27)	0·577
Postoperative mortality	37 (4·8)	1 (3)	0·710
Ascites	230 (29·9)	4 (13)	0·064§
Liver failure	23 (3·0)	1 (3)	0·606§
Abdominal collection	80 (10·4)	7 (23)	0·036§
Biliary leakage	73 (9·5)	6 (20)	0·108§
Infectious complication	205 (26·6)	8 (27)	0·996
Respiratory complication	320 (41·6)	9 (30)	0·258§
Confusion	71 (9·2)	4 (13)	0·516§
Renal insufficiency	71 (9·2)	4 (13)	0·516§
Haemorrhage	33 (4·3)	0 (0)	0·630§
Multiple organ failure	49 (6·4)	3 (10)	0·437§
Reoperation	48 (6·2)	1 (3)	0·516
Duration of surgery (min)*	360 (150–980)	348 (180–480)	0·591¶
Blood loss (ml)*	610 (50–7500)	623 (50–4500)	0·653¶
Transfusion	182 (23·7)	9 (30)	0·422
Hospital stay (days)*	13 (2–96)	12 (5–49)	0·871¶
After propensity score adjustment†	*n* = 190	*n* = 19	
Postoperative complications	129 (67·9)	15 (79)	0·438§
Dindo–Clavien grade I–II	103 (54·2)	11 (58)	0·758
Dindo–Clavien grade III–IV	21 (11·1)	4 (21)	0·204§
Postoperative mortality	5 (2·6)	0 (0)	0·474
Ascites	49 (25·8)	3 (16)	0·336
Liver failure	4 (2·1)	0 (0)	0·523
Abdominal collection	19 (10·0)	5 (26)	0·033
Biliary leakage	12 (6·3)	4 (21)	0·021
Infectious complication	55 (28·9)	7 (37)	0·473
Respiratory complication	68 (35·8)	6 (32)	0·714
Confusion	20 (10·5)	3 (16)	0·485
Renal insufficiency	14 (7·4)	3 (16)	0·200
Haemorrhage	7 (3·7)	0 (0)	0·393
Multiple organ failure	7 (3·7)	1 (5)	0·542§
Reoperation	9 (4·7)	1 (5)	0·922§
Duration of surgery (min)*	312 (150–660)	335 (180–480)	0·526¶
Blood loss (ml)*	586 (50–5200)	612 (50–4500)	0·627¶
Transfusion	42 (22·1)	5 (26)	0·684§
Hospital stay (days)*	13 (2–96)	13 (5–49)	0·772¶

Values in parentheses are percentages unless indicated otherwise; *values are median (range). †Propensity score adjustment was performed on variables that are likely to influence the choice of the approach, including: baseline characteristics (sex, age, American Society of Anesthesiologists fitness grade, body mass index), co-morbidities (diabetes, chronic obstructive pulmonary disease, ischaemic heart disease), presence of severe underlying fibrosis, indication for hepatectomy (malignant or benign disease, living donation), tumour characteristics (number, size), type of resection (right, left, extended right, extended left) and extent of resection (biliary and vascular reconstruction, associated hepatic and extrahepatic resection). ‡χ^2 test, except §Fisher's exact test and ¶Mann–Whitney *U* test.

respectively; $P = 0{\cdot}327$) and surgical margin width (mean 1·2 *versus* 1·0 cm; $P = 0{\cdot}470$).

Comparison of outcomes in patients who had conversion and those who had planned laparotomy

Comparison of the preoperative and operative characteristics of patients who had conversion and those who underwent planned laparotomy is provided in *Table S3* (supporting information). Before propensity score adjustment, these two groups were not comparable in terms of baseline characteristics and indications for surgery, as patients in the conversion group were significantly older (67·2 *versus* 55·4 years in the laparotomy group; $P < 0{\cdot}001$), more frequently had an ASA grade above II (13 *versus* 4·4 per cent respectively; $P = 0{\cdot}024$), BMI above 28 kg/m^2 (47 *versus* 17·3 per cent; $P < 0{\cdot}001$), metabolic syndrome (13 *versus* 3·5 per cent; $P < 0{\cdot}001$) or COPD (17 *versus* 2·6 per cent; $P < 0{\cdot}001$), and were more frequently operated on for malignant disease (90 *versus* 69·4 per cent; $P = 0{\cdot}015$). Conversely, there were no significant differences between these two groups regarding operative characteristics, apart from the rates of inflow clamping and abdominal drainage. After propensity score matching, the two groups were comparable in terms of baseline characteristics, indications for surgery and operative characteristics.

Table 4 summarizes the comparison of the postoperative course of patients who had conversion and patients who underwent planned laparotomy before and after propensity score adjustment. After propensity score adjustment, there was no significant difference in the rates of overall, major and pulmonary postoperative complications between the two groups. However, patients who underwent a conversion more frequently had abdominal collections and biliary leakage than those who had a planned laparotomy. Finally, matched patients in the conversion and planned laparotomy groups operated on for malignant disease had similar rates of surgical margin clearance (84 *versus* 80·9 per cent respectively; $P = 0{\cdot}693$) and surgical margin width (mean 1·3 *versus* 1·1 cm; $P = 0{\cdot}559$).

Discussion

In the present study, conversion during LMH occurred in 13·5 per cent of the patients. Patient age, existence of diabetes, raised BMI, large lesion size and associated biliary reconstruction were identified as risk factors for conversion. In this setting, conversion was associated with a worse postoperative outcome compared with fully laparoscopic liver resection, but provided almost the same outcomes as planned open major hepatectomy.

Intuitively, conversion would occur more frequently during the early experience of LMH. In the present study, however, the conversion rate was stable throughout the study period. The explanation for this may be twofold. First, at both centres, LMH was attempted only after a certain expertise in LLR had been acquired[28]. This finding emphasizes the necessary learning curve for LMH, even for surgeons who are familiar with laparoscopic minor liver resection. Second, indications for laparoscopy increased dramatically over time, with more complex procedures, more patients with increased BMI, as well as patients with large lesions. In these patients, exposure can sometimes be difficult in the upper part of the transection plane or even during final liver mobilization, as attested by the high incidence of conversion during the latest steps of the procedure rather than during pedicular dissection. Thus, even though it is likely that increasing expertise will help overcome traditional contraindications to the laparoscopic approach, such as the need for biliary or vascular reconstruction, the present results suggest that surgeons will still be confronted with considerable difficulties during parenchymal transection.

In patients undergoing LMH, the question of whether conversion leads to more postoperative complications than when conversion is not needed has, to date, remained unanswered. In colorectal surgery, it has been reported[29] that, although patients who underwent conversion experienced greater blood loss, increased time to first bowel movement and longer length of stay than those who did not, this did not result in increased rates of transfusion or postoperative complications. In the present study, as in previous ones[16], the main indication for conversion was haemorrhage. In this context, patients who had a conversion logically experienced more blood loss and had higher transfusion rates than matched patients who did not. Similarly, patients who underwent conversion had more postoperative complications, especially pulmonary complications, and a trend towards a longer hospital stay than patients who did not undergo conversion. This finding is probably related to the fact that the majority of the patients underwent conversion through subcostal or J-shaped incisions. These incisions require transection of abdominal muscles and prolonged retraction of the right hemidiaphragm, and result in painful limitation of inhalation. In addition, the majority of conversions occurred during parenchymal transection after considerable operating time. Hence, to improve the postoperative tolerance and limit the negative effects of both conversion and prolonged surgery[30], a hybrid approach with laparoscopic pedicular dissection and open parenchymal transection using a minilaparotomy through a midline incision facilitated by a hanging manoeuvre[31–33] could be attractive in the presence of risk factors for conversion. This seems particularly relevant for large lesions, where extraction of the resected specimen may be challenging.

Determining whether conversion is associated with impaired outcomes compared with planned laparotomy is of crucial importance as it could represent a strong argument against the laparoscopic approach in patients requiring major hepatectomy. In the present study, however, patients who underwent conversion experienced similar blood loss and transfusion rates as matched patients who had planned laparotomy. This result suggests that the combination of low central venous pressure and pneumoperitoneum limits the consequences of vascular injury[11,34] to some extent, and allows conversion to be performed safely in difficult situations. In the same way, overall postoperative complications and hospital stay were identical between patients who had conversion and those who underwent laparotomy, similar to what is observed in colorectal surgery[29,35], and thus further confirms that a considerable amount of the morbidity related to conversion was the consequence of the incision itself. However, it should be noted that patients who had conversion experienced significantly higher rates of postoperative biliary leakage and abdominal collection than matched patients who had a laparotomy. Interestingly, this striking difference was not observed between patients who underwent conversion and those who did not. Therefore, whether this finding is related to the conversion itself, or rather represents an inherent limitation of the laparoscopic approach, will have to be assessed in further studies. Nevertheless, this observation highlights that specific emphasis should be given to control of bile leaks in patients having laparoscopic major resection, particularly in the event of conversion. Likewise, increased awareness with liberal use of abdominal CT is required during the postoperative period for early detection of deep infectious complications in these patients.

The present study has several limitations. First, its retrospective nature and the relatively small number of events, especially after propensity score matching, might have led to insufficient statistical power in the analysis of the consequences of conversion on the postoperative course of patients, with the possibility of a type II error. In addition, the limited number of patients experiencing conversion precluded the drawing of solid conclusions regarding the impact of both timing and type of conversion on the postoperative results. Second, data regarding initial LMH procedures were not available for one of the centres. This may have led to underestimation of the overall rates of conversion. However, as the conversion rate appears to parallel the complexity of the cases, it is likely that conversion does not truly reflect the learning curve in laparoscopic major liver resection, which limits the consequences of this bias. Finally, patients undergoing open major hepatectomy in centres 1 and 2 were not analysed. As no patient had major LLR at centre 3 during the study period, potential corresponding controls were more likely to be found in this centre than in centres 1 and 2, where open resection was performed only when laparoscopy was contraindicated.

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Supporting information

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

Fig. S1 Flow chart for the study (TIFF file)

Table S1 Details of preoperative, operative and postoperative characteristics of patients who underwent conversion (Word document)

Table S2 Univariable and multivariable analyses of the risk factors for postoperative complications (Word document)

Table S3 Comparison of the preoperative and operative characteristics of patients who underwent conversion and patients who had planned laparotomy (Word document)