Surg Endosc (2016) 30:3709–3719
DOI 10.1007/s00464-015-4666-z

Incidence, risk factors and consequences of bile leakage following laparoscopic major hepatectomy

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Received: 6 September 2015 / Accepted: 3 November 2015 / Published online: 17 November 2015

Abstract

Background Bile leakage (BL) remains a common cause of major morbidity after open major liver resection but has only been poorly described in patients undergoing laparoscopic major hepatectomy (LMH). The present study aimed to determine the incidence, risk factors and consequences of BL following LMH.

Methods All 223 patients undergoing LMH between 2000 and 2013 at two tertiary referral centres were retrospectively analysed. BL was defined according to the International Study Group of Liver Surgery, and its incidence and consequences were assessed. Risk factors for BL were determined on multivariate analysis.

Results BL occurred in 30 (13.5 %) patients, and its incidence remained stable over time ($p = 0.200$). BL was diagnosed following the presence of bile into the abdominal drain in 14 (46.7 %) patients and after drainage of symptomatic abdominal collections in 16 (53.3 %) patients without intra-operative drain placement. Grade A, B and C BL occurred in 3 (10.0 %), 23 (76.6 %) and 4 (13.4 %) cases, respectively. Interventional procedures for BL included endoscopic retrograde cholangiography, percutaneous and surgical drainage in 10 (33.3 %), 23 (76.7 %) and 4 (13.3 %) patients, respectively. BL was associated with significantly increased rates of symptomatic pleural effusion (30.0 vs. 11.4 %, $p = 0.006$), multiorgan failure (13.3 vs. 3.6 %, $p = 0.022$), postoperative death (10.0 vs. 1.6 %, $p = 0.008$) and prolonged hospital stay (18 vs. 8 days, $p < 0.001$). On multivariable analysis, BMI > 28 kg/m^2 (OR 2.439, 95 % CI 1.878–2.771, $p = 0.036$), history of hepatectomy (OR 1.675, 95 % CI 1.256–2.035, $p = 0.044$) and biliary reconstruction (OR 1.975, 95 % CI 1.452–2.371, $p = 0.039$) were significantly associated with increased risk of BL.

Conclusions and relevance After LMH, BL occurred in 13.5 % of the patients and was associated with significant morbidity. Patients with one or several risk factors for BL should benefit intra-operative drain placement.

Keywords Bile leakage · Laparoscopic major hepatectomy · Postoperative complications · Abdominal drainage

Electronic supplementary material The online version of this article (doi:10.1007/s00464-015-4666-z) contains supplementary material, which is available to authorized users.

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Among various postoperative complications following liver resection, bile leakage (BL) still represents a common cause of major morbidity, favouring the onset of several other complications such as intra-abdominal infection [1, 2], gastrointestinal bleeding [2], impaired regeneration [3], thrombo-embolic events [1]. Furthermore, BL is consistently associated with prolonged hospital stay [2, 4]. In most recent series, BL has been reported to occur in 3.6–10 % [1, 2, 4–10] of patients following hepatectomy depending on several factors. In particular, it seems that both extent [1, 4] and complexity [4, 11, 12] of liver resection are critical risk factors for the development of BL.

During the past decade, refinements in laparoscopic tools and surgical skills have allowed surgeons to perform always more complex laparoscopic liver resections [13, 14], including laparoscopic major hepatectomies (LMH) [15, 16]. In this setting, several studies have now reported that laparoscopy was associated with decreased rates of major postoperative complications [17, 18], diminished blood loss [17] and shorter hospital stay [17] in patients undergoing major hepatectomy, while respecting fundamental oncologic principles at the same time [19].

To date, however, no series has specifically focused on BL following laparoscopic liver resection. Furthermore, the series evaluating the postoperative results of laparoscopic liver resections, including major ones, have reported troublingly low rates of BL, ranging from 0 to 7.1 % [15, 20–22]. Whether these results account for a true benefit of laparoscopy in decreasing the incidence of BL or rather account for insufficient data collection and analysis remains unclear but nevertheless require further investigation.

Hence, the present study aims at evaluating the incidence, risk factors and consequences of BL in patients undergoing LMH at two tertiary referral units.

Materials and methods

Patient selection and data sources

The current study included all patients undergoing full laparoscopic major (≥3 contiguous Couinaud segments [23] right or left liver resection at Institut Mutualiste Montsouris (centre 1) from 2000 to 2013 and at Hôpital Saint-Antoine (centre 2) from 2009 to 2013. No patient underwent a planned "hand-assisted" or "hybrid" approach. For centre 2, the first major laparoscopic liver resections were performed in 2007, but a relocation of the surgical team to another hospital in 2009 prevented collection of data prior to 2009. The collected data were retrieved from prospectively maintained databases and included baseline patient's characteristics such as demographic data, preoperative risk factors and comorbidities, type of preoperative management, operative characteristics, pathologic data and postoperative outcomes. The local institutional review board in each centre approved this study.

Surgical technique

All procedures were performed by at least one senior surgeon. Liver transection was performed under low (<5 mmHg) central venous pressure [24]. Briefly, LMH was performed using five or six ports depending on the surgical procedure and operator preference, as described [19, 25]. Laparoscopic ultrasonography was routinely used to guide the resection. The operative technique was similar to open surgery: isolation and division of hepatic inflow, absence of mobilization of the right liver prior to transection and subsequent transection of liver parenchyma. Clamping of the hepatic inflow pedicle was not routinely performed during this step, and the Pringle manoeuvre was only used in case of bleeding. Energy sources and parenchymal division techniques varied throughout the study period and included ultrasonic dissector or harmonic scalpel [primarily SonoSurg® and more recently Harmonic® (Ethicon Endo-Surgery, Inc, Cincinnati, OH) or Thunderbeat® (Olympus Co, Tokyo, Japan)]. For right-sided resections, when parenchyma transection reached the hilar plate, segment I was divided along the right aspect of the inferior vena cava to allow dissection of the corresponding bile duct and hilar plate. The right or left bile duct was then taped, closed using either a large secured clip, a running suture or a stapler depending upon the surgeons' preference 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 7- to 11-cm suprapubic incision without muscle section. This incision was immediately closed and the abdomen reinsufflated to confirm haemostasis and absence of bile leaks. BL test using methylene blue or air injection through the cystic drain was not routinely performed. Abdominal drainage was only used if there was concern about intra-operative bile control or the adequacy of haemostasis.

Selection criteria for the use of the laparoscopic approach evolved over time and varied according to centre, but patients qualified for LMH only if lesions were far from the liver hilus, the hepatocaval junction and the inferior vena cava. All lesions had to be well clear of the midplane 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. While the laparoscopic approach was initially avoided 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.

Postoperative management

After surgery, a physician saw all patients daily until hospital discharge. Liver function tests were measured on postoperative days (POD) 1, 3, 5, 7 and 10. Chest radiography was routinely performed on POD 1 and 3 in both centres. A thoraco-abdomino-pelvic CT scan with intravenous contrast injection was performed selectively in case of suspected abdominal or thoracic complication.

Since abdominal drainage was not routinely placed during the procedure, BL could be diagnosed either: (1) classically with a bilirubin concentration in the drainage fluid more than three times the serum total bilirubin level in the drain when present on POD3, as defined by the International Study Group of Liver Surgery (ISGLS) [26], or (2) considering the presence of bile after percutaneous or surgical drainage of a collection as diagnosed by ultrasound or CT scan in symptomatic patients. The severity of BL was divided into three groups according to the ISGLS definition [26]. Grade A included BL with little or without any impact in the clinical management, grade B included BL requiring a change in the clinical management or BL lasting >7 days regardless of the impact on the clinical management, and grade C included BL requiring a repeat laparotomy.

Conservative management of BL with prolonged drainage and antibiotic treatment in the event of persistent fever was systematically attempted in patients who had intra-operative placement of an abdominal drain. Percutaneous drainage was performed in case of persistent intra-abdominal bile collection, or as primary treatment for suspected BL in patients who did not have intra-operative placement of an abdominal drain. In case of persistent biliary leakage, endoscopic retrograde cholangio-pancreatography (ERCP) with sphincterotomy and selective stent placement was performed. If non-surgical treatment proved ineffective, if the clinical situation of the patient worsened, or if biliary peritonitis developed, a relaparotomy was considered.

Other specific liver-related complications were categorized as follows: liver failure was defined according to the '50–50 criteria' on postoperative day 5 [27]; ascites was defined as abdominal drainage output of more than 10 ml/kg/day after the third postoperative day [28]; and haemorrhage was defined as a drop of haemoglobin level >3 g/dl after the end of surgery compared to postoperative baseline level and/or any postoperative transfusion of packed red blood cell units for a falling haemoglobin and/or the need for invasive reintervention [29].

Postoperative complications were stratified according to the Dindo–Clavien classification [30], which defines major complications by a grade ≥3. Complications and operative mortality were considered as those occurring within 90 days of surgery, or at any time during the postoperative hospital stay.

Statistical analysis

Quantitative variables are expressed as median (range), and qualitative variables are expressed as frequencies (percentages). A Student *t* test or Mann–Whitney *U* test was used for intergroup comparisons of quantitative variables as appropriate, whereas a Chi-square test or Fisher's exact test was used to compare categorical data. The probability of experiencing BL was estimated using a multivariable logistic regression model. All variables that differed significantly in univariable analysis ($p < 0.1$) when comparing the two groups were included in the logistic model, and backward selection was applied. All statistical analyses were performed with SPSS version 20.0 (SPSS Inc., an IBM Company, Chicago, IL, USA).

Results

Patients' characteristics

A total of 223 patients underwent LMH during the study period including 135 (60.5 %) males. Median age was 63.5 (23.9–86.2) years. Median BMI was 24.9 (15.9–35.5) kg/m^2, and 54 (24.2 %) patients had a BMI > 28 kg/m^2. A previous minor liver resection was performed in 33 (14.7 %) patients. Indications for liver resection were malignant disease in 197 (88.3 %) patients, including colorectal liver metastases in 112 (50.2 %), HCC in 44 (19.7 %), cholangiocarcinoma in 27 (12.1 %) and other types of malignancy in 14 (6.3 %) patients. A diseased underlying liver was present in 89 (39.9 %) patients. Severe (F3–F4) fibrosis was present in 34 (15.2 %) patients, including in 23 operated for HCC, in 6 operated for colorectal liver metastases, in 2 operated for cholangiocarcinoma and in 3 operated for other types of lesions. Significant (>30 %) steatosis was present in 39 patients, including in 24 patients operated for colorectal liver metastases, in 8 operated for HCC, in 1 operated for cholangiocarcinoma and in 6 operated for other types of lesions. Significant (≥grade 2) sinusoidal obstruction syndrome was present in 16 (7.2 %) patients, all operated for colorectal liver metastases. Preoperative portal vein embolization (PVE) and transarterial chemoembolization (TACE) were performed in 45 (20.2 %) and 13 (5.8 %)

patients, respectively. A total of 11 (4.9 %) patients underwent sequential TACE–PVE.

Major right-sided resections were performed in 160 (71.7 %) patients, and 33 (14.8 %) patients had removal of more than four hepatic segments. Segment IV was removed in 83 (37.2 %) patients. Associated wedge resection or radiofrequency ablation in the contralateral lobe was performed in 24 (10.8 %) and 7 (3.1 %) patients, respectively. Biliary and portal reconstructions were performed in 8 (3.6 %) and 1 (0.4 %) patients, respectively. Extra-hepatic procedures were performed in 16 (7.2 %) patients including diaphragmatic resections in 9 (4 %) patients, colonic resection in 3 (1.3 %) patients, and distal pancreatectomy, duodenal resection, right adrenal gland resection and right nephrectomy in one (0.4 %) patient each. Median blood loss was 200 (50–4500) ml, with 44 (19.7 %) patients experiencing blood loss >500 ml and 29 (13.0 %) patients requiring transfusion of red blood cells. An abdominal drain was placed in 63 (28.3 %) patients, including in 19 of the 44 patients (43.2 %) with intra-operative blood loss >500 ml.

Postoperative course

In the whole cohort, 6 (2.7 %) patients died during the postoperative period and 117 (52.5 %) patients experienced postoperative complications, including major complications in 50 (22.4 %) patients. Pulmonary complications occurred in 39 (17.5 %) patients, BL in 30 patients (13.5 %), postoperative ascites in 16 (7.2 %) patients, liver failure in 8 (3.6 %) patients and haemorrhage in 2 (0.9 %) patients. Infectious postoperative complications occurred in 49 (22.0 %) patients. An abdominal collection was present on postoperative CT scan in 48 (21.5 %) patients. Drainage of these collections was performed in 29 symptomatic patients, including 27 patients with BL and two patients with non-biliary collections (one patient with haematoma and one patient with abscess). Among the 27 patients drained for BL, 11 had intra-operative abdominal drainage placement. Altogether, a total of 19 patients (11.9 % of patients without intra-operative drain placement) had asymptomatic postoperative abdominal collections that did not require drainage.

Incidence and characteristics of bile leakage

The rates of BL were similar rates between centre 1 and centre 2 (13.6 vs. 13.0 %, $p = 0.904$). Figure 1 shows the evolution in the rates of BL according to the year. When the experience of each centre was divided in two periods of equal numbers of procedures (early vs. late), there was a non-significant trend in the increase in the rate of BL over time (11.4 vs. 19.4 %, $p = 0.200$).

The median delay from surgery to the occurrence of BL was 7 (2–12) days. BL was diagnosed following the presence of bile into the operatively placed abdominal drain in 14 (46.7 %) patients (including 3, 10 and 1 grade A, B and C BL, respectively) at a median of 5 (2–10) days, and after drainage of symptomatic abdominal collections in 16 (53.3 %) patients without intra-operative abdominal drain placement (including 0, 14 and 2 patients, respectively) at a median of 8 (4–12) days ($p = 0.246$).

Sixteen (53.3 %) patients with BL experienced other associated complications. The details of these complications and their comparison with patients who did not experience BL are provided in Table 1. Patients with BL experienced increased rates of acute respiratory insufficiency (30.0 vs. 3.1 %, $p < 0.001$), symptomatic pleural effusion (30.0 vs. 11.4 %, $p = 0.006$), acute renal insufficiency (13.3 vs. 3.1 %, $p = 0.012$), reoperation (2.6 vs. 13.3 %, $p = 0.005$) and multiorgan failure (13.3 vs. 3.6 %, $p = 0.022$), compared with those without BL. The presence of BL was also associated with increased rate of mortality (10.0 vs. 1.6 %, $p = 0.008$) and prolonged hospital stay (18 vs. 8 days, $p < 0.001$).

BL were classified as grades A, B and C in 3 (10.0 %), 23 (76.7 %) and 4 (13.3 %) cases, respectively. Management was conservative with simple surveillance in 3 (10.0 %) patients, and 27 (90.0 %) patients required interventional procedures. Percutaneous drainage of bile collections was performed in 23 (76.7 %) patients, and 4 (13.3 %) patients underwent surgical drainage. ERCP was performed in 10 (33.3 %) cases, including stent placement in 4 (13.3 %) patients. Overall, 26 (86.7 %) patients with BL evolved towards healing after a median of 24 (2–93) days, and one (3.3 %) experienced biliary stenosis requiring secondary hepatico-jejunostomy confection. Three (10.0 %) patients with BL died postoperatively. All had grade B BL.

Risk factors for bile leakage

Table 2 shows the results of univariable and multivariable analyses of the risk factors for BL. On multivariable analysis, a BMI > 28 kg/m^2 (OR 2.439, 95 % CI 1.878–2.771, $p = 0.036$), a previous history of hepatic surgery (OR 1.675, 95 % CI 1.256–2.035, $p = 0.044$), an associated wedge resection (OR 2.330, 95 % CI 1.796–3.014, $p = 0.031$) and an associated biliary reconstruction (OR 1.975, 95 % CI 1.452–2.371, $p = 0.039$) were significantly associated with increased risk of postoperative BL.

Finally, as shown in supplementary Table 1, the type of underlying liver (severe fibrosis, significant steatosis, significant sinusoidal obstruction syndrome or no underlying liver disease) did not influence the occurrence of overall

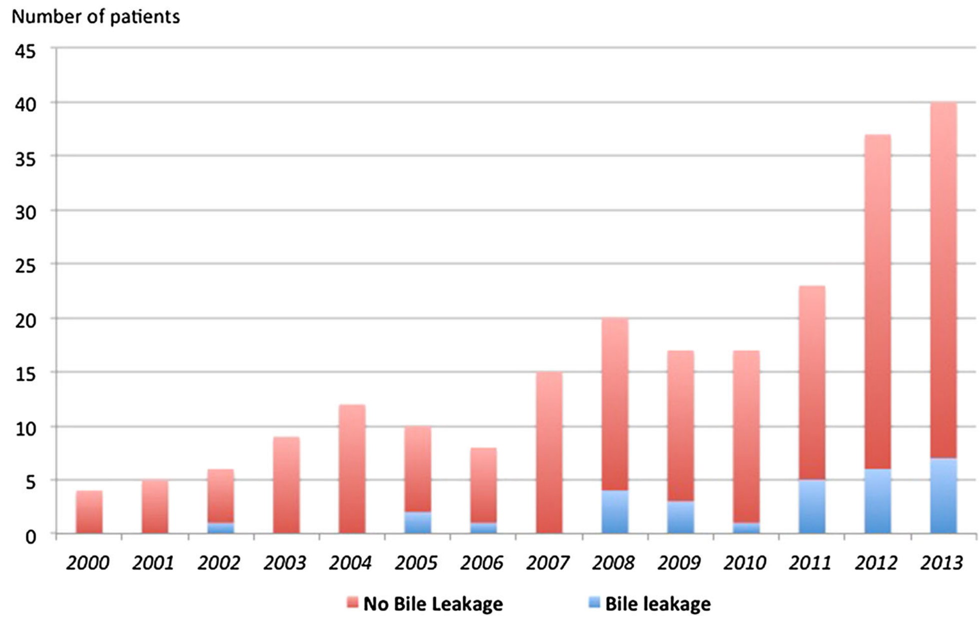

Fig. 1 Bile leakage according to the year

Table 1 Complications associated with bile leakage

	No bile leakage $n = 193$	Bile leakage $n = 30$	p
Ascites (%)	13 (6.7)	3 (10.0)	0.519
Liver failure (%)	8 (4.1)	0 (0.0)	0.256
Fever (%)	33 (17.1)	14 (46.7)	<0.001
Infectious complication (%)	35 (18.1)	14 (46.7)	<0.001
Pulmonary complications (%)	30 (15.5)	9 (30.0)	0.052
Pulmonary infection (%)	11 (5.7)	0 (0.0)	0.180
Acute respiratory insufficiency (%)	6 (3.1)	9 (30.0)	<0.001
Symptomatic pleural effusion (%)	22 (11.4)	9 (30.0)	0.006
Atelectasia (%)	12 (6.2)	1 (3.3)	0.530
Pulmonary embolism (%)	2 (1.0)	1 (3.3)	0.310
Confusion (%)	6 (3.1)	3 (10.0)	0.074
Acute renal insufficiency (%)	6 (3.1)	4 (13.3)	0.012
Haemorrhage (%)	2 (1.0)	0 (0.0)	0.575
Reoperation (%)	5 (2.6)	4 (13.3)	0.005
Multiorgan failure (%)	7 (3.6)	4 (13.3)	0.022

($p = 0.964$) and severe ($p = 0.836$) postoperative complications, mortality ($p = 0.696$), liver failure ($p = 0.396$), bile leakage ($p = 0.802$) and ascites ($p = 0.468$).

Discussion

In the present study, BL occurred in 13.5 % of patients undergoing LMH, which is consistent with previous series of major open hepatectomies [1, 4, 8, 31–35] (Table 3a). These BL were graded as B or C in as much as 90 % of the patients, leading to increased rates of associated postoperative complications and a mortality rate of 10 %.

In the current study, the rate of BL remained stable over time with a non-significant trend towards an increased incidence in the most recent years. This result rules out any "learning curve effect" but could rather account for an increased complexity of the procedures that have been undertaken recently [36]. Nonetheless, the observed incidence of BL was clearly higher than those reported in previous series of laparoscopic liver resections including major ones [15, 20–22, 25, 37–44] (Tables 3b, c). This finding is likely a consequence of the fact that none of these previous studies had specifically focused on BL following LMH and that data collection regarding this complication were probably limited. Furthermore, the absence of

Table 2 Univariable and multivariable analyses of the risk factors for bile leakage

	No bile leakage $n = 193$	Bile leakage $n = 30$	p	HR	95 % CI	p
Preoperative characteristics						
Male (%)	121 (62.9)	14 (46.7)	0.095	0.873	0.438–2.651	*0.263*
Age (years)[a]	63.8 (24.1–86.2)	62.5 (23.9–84.0)	0.374			
>75 years (%)	32 (16.6)	3 (10.0)	0.357			
ASA score ≤2 (%)	154 (79.8)	23 (76.7)	0.694			
Diabetes (%)	26 (13.5)	3 (10.0)	0.599			
Hypertension (%)	53 (27.5)	10 (33.3)	0.506			
Dyslipidemia (%)	31 (16.1)	8 (26.7)	0.155			
BMI > 28 (kg/m^2) (%)	41 (21.2)	13 (43.3)	0.009	2.439	1.878–2.771	*0.036*
Metabolic syndrome (%)	11 (5.7)	4 (13.3)	0.12			
Cardio-respiratory comorbidity (%)	36 (18.7)	7 (23.3)	0.545			
Coronary heart disease (%)	19 (9.8)	2 (6.7)	0.579			
COPD (%)	16 (8.3)	4 (13.3)	0.368			
Tobacco (%)	53 (27.5)	10 (33.3)	0.506			
Previous abdominal surgery (%)	114 (59.1)	20 (66.7)	0.429			
Colorectal surgery (%)	81 (42.0)	10 (33.3)	0.37			
Hepatic surgery (%)	25 (13.0)	8 (26.7)	0.049	1.675	1.256–2.035	*0.044*
Others (%)	13 (6.7)	3 (10.0)	0.519			
Underlying liver disease (%)						
Alcohol	36 (18.7)	7 (23.3)	0.545			
Viral infection	20 (10.4)	0 (0.0)	0.065	0.631	0.410–1.191	*0.201*
Iron overload	4 (2.1)	0 (0.0)	0.043			
Severe fibrosis	29 (15.0)	5 (16.7)	0.816			
Steatosis >30 %	32 (16.6)	7 (23.3)	0.365			
Pathology (%)						
Malignant disease	169 (87.6)	28 (93.3)	0.36			
HCC	38 (19.7)	6 (20.0)	0.968			
Cholangiocarcinoma	21 (10.9)	6 (20.0)	0.154			
Colorectal liver metastases	99 (51.3)	13 (43.3)	0.417			
Other	11 (5.7)	3 (10.0)	0.366			
Benign disease	24 (12.4)	2 (6.7)	0.36			
Liver cell adenoma	5 (2.6)	1 (3.3)	0.815			
Focal nodular hyperplasia	5 (2.6)	0 (0.0)	0.373			
Mucinous cystadenoma	4 (2.1)	1 (3.3)	0.664			
Living donor	2 (1.0)	0 (0.0)	0.575			
Other	8 (4.1)	0 (0.0)	0.256			
Bilobar disease	22 (10.9)	9 (30.0)	0.006	1.833	0.894–3.062	*0.173*
Single lesion	102 (52.8)	16 (53.3)	0.961			
Tumour diameter >10 cm	21 (10.9)	6 (20.0)	0.154			
Preoperative management (%)						
Preoperative chemotherapy	78 (40.4)	9 (30.0)	0.277			
>6 cycles	56 (29.0)	7 (23.3)	0.52			
Oxaliplatin	77 (39.9)	9 (30.0)	0.3			
Irinotecan	22 (11.4)	3 (10.0)	0.821			
Targeted therapy	18 (9.3)	4 (13.3)	0.493			
Preoperative TACE	13 (6.7)	0 (0.0)	0.143			
Preoperative PVE	39 (20.2)	6 (20.0)	0.979			

Table 2 continued

	No bile leakage $n = 193$	Bile leakage $n = 30$	*p*	HR	95 % CI	*p*
Intra-operative characteristics						
>4 resected segments (%)	27 (14.0)	6 (20.0)	0.388			
Right-sided hepatectomy (%)	140 (72.5)	20 (66.7)	0.506			
Removal of segment IV	68 (35.2)	15 (50.0)	0.12			
Associated RFA (%)	5 (2.6)	2 (6.7)	0.234			
Associated wedge resection (%)	17 (8.8)	7 (23.3)	0.017	2.33	1.796–3.014	*0.031*
Biliary reconstruction (%)	5 (2.6)	3 (10.0)	0.042	1.975	1.452–2.371	*0.039*
Vascular reconstruction (%)	0 (0.0)	1 (3.3)	0.011	–	–	–
Extra-hepatic procedure (%)	15 (7.8)	1 (3.3)	0.381			
Transection device						
Ultrasonic dissector (%)	146 (75.6)	23 (76.7)	0.904			
Harmonic scalpel (%)	47 (24.4)	7 (23.3)	0.904			
Inflow clamping (%)	24 (12.4)	5 (16.7)	0.522			
Conversion (%)	24 (7.3)	6 (20.0)	0.259			
Blood loss (ml)*	250 (10–900)	200 (50–4500)	0.34			
Transfusion (%)	26 (13.5)	3 (10.0)	0.599			
Surgery duration (mn)*	300 (100–480)	300 (120–540)	0.713			
Abdominal drain placement (%)	49 (25.4)	14 (46.7)	0.016	1.629	0.837–1.972	0.243
R1/R2 resection (%)	9 (4.7)	7 (23.3)	<0.001	1.326	0.919–1.733	0.152

The first *p* value refers to the significance on univariate analysis and the second *p* value (after the 95 % confidence interval (95 % CI)) refers to the significance on multivariate analysis

ASA American Society of Anaesthesiology, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *HCC* hepatocellular carcinoma, *TACE* transarterial chemoembolization, *PVE* portal vein embolization, *RFA* radio frequency ablation

[a] Expressed as mean (range)

systematic use of the consensual definition for BL [26] also obviously precluded relevant analysis of both incidence and consequences of the risk factors of BL following LMH.

Indeed, with several series focusing on BL following open liver resections, a uniform and international definition of BL was proposed in 2011 [26]. One of the limitations of this definition remains the assessment of asymptomatic BL in patients who did not have intra-operative drain placement. In the present study, 72.7 % of the patients did not receive intra-operative abdominal drain and 19 of them experienced asymptomatic postoperative collections, which did not require secondary drainage. Hence, it is possible that some of these collections were in fact asymptomatic bilomas, which resolved spontaneously. In this setting, the 13.5 % incidence of BL observed in the current study may probably represent an underestimation of the true incidence of BL according to the ISGLS definition, especially regarding the rates of grade A BL. Likewise, this low rate of grade A fistula might have artificially overestimated the severity of BL in patients undergoing LMH. Nevertheless, it should be acknowledged that BL were responsible of half the postoperative deaths and favoured the onset of various complications, emphasizing the need to improve both their diagnosis and management.

While systematic routine placement of an abdominal drain during surgery may allow early detection of BL, it may also represent a risk factor for ascending and secondary infection of the collections [45], leading to increased severity of BL. Hence, previous studies of open hepatectomies highlighted that a prophylactic drain should be considered following hepatic resection for patients with positive BL test and operation time ≥360 min [46]. Yet, these factors do not seem reliable in the specific setting of LMH. Even though the usefulness of BL test in patients undergoing liver resection is still a matter of ongoing debate [8, 47, 48], the evaluation of its relevance in predicting BL in patients undergoing LMH would therefore require specific measures such as intravenous injection of indocyanine green with use of fluorescence [49] or 5-aminolevulinic acid-mediated photodynamic diagnosis [50] to improve its feasibility. Of course the present study did not aim at evaluating the effectiveness or consequences of prophylactic abdominal drainage in patients undergoing LMH. In this setting, the fact that only 21.4 % (3/14) of patients with intra-operative drain placement presenting with BL were managed conservatively could question its benefit. However, it should be noted that more

Table 3 Incidence and risk factors for BL after open major hepatectomy (OMH), laparoscopic liver resection (LLR) and laparoscopic major hepatectomy (LMH) in relevant recent series

Author, year	Number of patients	Type of resection	Overall bile leakage rate	Grade A[a]	Grade B[a]	Grade C[a]	Risk factors
a. After open major hepatectomy							
Capussotti et al. [31]	254[b]	OMH	5.5 %	–	–	–	–
Li et al. [32]	137	OMH	13.9 %	–	–	–	White test, Klatskin tumour, biliary-enteric anastomosis, and longer operation time
Yoshioka et al. [33]	106[b]	OMH	6.5 %	–	–	–	–
Rahbari et al. [34]	170[b]	OMH	Grade B/C: 26.9 %	–	100 %	–	
Zimmitii et al. [4]	1503[b]	OMH	6.9 %	–	–	–	–
Zimmitii et al. [8]	223	OMH	6.7 %	33.0 %	67.0 %	Extended hepatectomy, caudate resection, no air leak test	
Guillaud et al. [1]	539[b]	OMH	10.8 %	–	–	–	–
Zheng et al. [35]	297	OMH	30.6 %	26.4 %	70.3 %	3.3 %	Grade B/C: elevated ALT, positive bile culture, hilar bile duct plasty, bilio-enteric anastomosis, laparoscopy
b. After laparoscopic liver resection (all types)							
Koffron et al. [37]	300	LLR	0.8 %[C]	–	–	–	–
Chang et al. [38]	36	LLS	0 %	0 %	0 %	0 %	–
Nguyen et al.[20]	2804	LLR	1.5 %	–	–	–	–
Nguyen et al. [21]	314	LLR	0 %	–	–	–	–
Cannon et al. [39]	300	LLR for CLM	5.3 %	–	–	–	–
Soubrane et al. [40]	351	LLR for HCC	2 %	–	–	–	–
Tranchart et al. [22]	140	LLR	3.6 %	0 %	40 %	60 %	–
c. After laparoscopic major hepatectomy							
Dagher et al. [15]	210	LMH	6.2 %	–	–	–	–
Cai et al. [41]	19	LLH for hepatolithiasis	0 %	–	–	–	
Tu et al. [42]	28	LLH for hepatolithiasis	7.1 %	–	–	–	–
Belli et al. [25]	82	LLH	Grade B/C: 1.2 %	–	0 %	100 %	–
Namgoong et al. [43]	37	LLH for hepatolithiasis	0 %	0 %	0 %	0 %	–

Table 3 continued

Author, year	Number of patients	Type of resection	Overall bile leakage rate	Grade A[a]	Grade B[a]	Grade C[a]	Risk factors
Ye et al. [44]	46	LLH for hepatolithiasis	6.5 %	–	–	–	–

OMH major open hepatectomy, *LLR* laparoscopic liver resection, *LLS* left lateral sectionectomy, *CLM* colorectal liver metastases, *HCC* hepatocellular carcinoma, *LMH* laparoscopic major hepatectomy, *LLH* laparoscopic left hepatectomy

[a] Expressed as percentage of bile leakage

[b] These series did not specifically focus on major hepatectomies but the number of patients undergoing major hepatectomy and their corresponding BL rates were available

[c] For full laparoscopic liver resections

than half of the patients with BL did not receive placement of an abdominal drain during the procedure. Hence, in the absence of practical predictor of their usefulness, it seems reasonable to recommend the placement of an abdominal drain in patients with one or several risk factors for BL.

Indeed, the present study identified four risk factors for postoperative BL, namely an elevated BMI, a previous history of hepatic surgery, an associated wedge resection and an associated biliary reconstruction. The increased risk of BL in patients undergoing repeated hepatectomy [4, 33] and bilio-enteric anastomosis [4, 32, 35] has been reported previously and is therefore not surprising. On the opposite, even though no clear explanation could be found, the current study highlighted that apart from patients with traditional risk factors for BL, those with elevated BMI and requiring contralateral resection should also be scrupulously screened for BL at the end of parenchymal transection in the specific setting of LMH.

Naturally, the current study has several limitations. Above all, this is a retrospective study covering a long time period during which the definition of BL has evolved. Hence, biased estimations of the rate and the severity of BL in patients undergoing LMH preclude a relevant comparison with patients undergoing open major hepatectomies. However, it should be noted that the 10 % overall rate of grade B/C BL was consistent with those reported in most recent series focusing on BL after open major hepatectomies and therefore represents a valuable indicator of the incidence of clinically significant BL in patients undergoing LMH. Furthermore, we could neither evaluate the influence of the type of closure of the bile duct and hilar plate on the occurrence of BL, nor assess the impact of the location of BLs on their severity and management. However, the present study represents the first one specifically focusing on BL following LMH and we feel that these questions would be better answered in dedicated studies.

Author contributions Study concept and design: Soubrane, Fuks, Cauchy, Gayet; Acquisition of data: Nomi, Schwarz, Belgaumkar, Fuks, Cauchy; Analysis and interpretation of data: Cauchy, Fuks, Gayet, Soubrane; Drafting of the manuscript: Cauchy, Fuks, Soubrane, Gayet; Critical revision of the manuscript: Fuks, Cauchy, Soubrane, Gayet, Scatton; Statistical analysis: Cauchy, Fuks, Study supervision: Soubrane, Fuks, Cauchy, Gayet.

Compliance with ethical standards

Disclosures François Cauchy, David Fuks, Takeo Nomi, Lilian Schwarz, Ajay Belgaumkar, Olivier Scatton, Olivier Soubrane and Brice Gayet have no conflicts of interest or financial ties to disclose.

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