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ORIGINAL ARTICLE

Risk factors for bile leakage after liver resection for neoplastic disease

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Abstract
Biliary leakage (BL) remains the most frequent and feared complication after hepatoresective surgery. Placement of the abdominal drainage at the end of liver surgery remains controversial due to the delicate balance between risks and potential benefits in case of BL. The study was aimed to detect possible risk factors for BL occurrence after liver surgery. We enrolled all oncologic patients who underwent liver resection from June 2016 to March 2021. BL was diagnosed according to the ISGLS definition. We have examined demographic characteristics of the patients, type of neoplasia, presence of cirrhosis, neoadjuvant chemotherapy and type of intervention. Uni- and multivariable analyses were performed to assess the predictive value of potential predictor of BL. A total of 379 patients were enrolled in the study, 16 (4.2%) of which developed BL. Among others, at univariate analysis the occurrence of BL was found to be associated with bilio-digestive anastomosis (OR: 9.75, C.I. 2.7–34.7, $p<0.001$) and neoadjuvant chemotherapy (OR: 0.09, C.I 0.01,–0.88, $p=0.039$). Multivariable analysis selected the body mass index (OR: 1.21, 95%C.I.: 1.04–1.41, $p=0.015$), anatomical resection (OR: 8.35, 95% C.I.: 2.01–34.74, $p=0.004$), and blood loss (OR: 1.09, 95%C.I.: 1.05–1.13, $p<0.001$). Identification of patients at greater risk of BL can help in the choice of positioning the drainage at the end of liver surgery.

Keywords Liver resection · Bile leakage · Post-hepatectomy complications · Postoperative drainage

Introduction

Over the past 25 years, hepatic resection has evolved from a high-risk, resource-intensive procedure with limited application to a safe and commonly performed operation, with broad indications. In recent years, thanks to scientific studies and experience in the field, it has been possible to note a significant improvement in the perioperative outcome, such as reduced mortality, blood loss, transfusion rates and hospital stays. Despite the advances, the appearance of biliary leakage (BL) occurs in 4–17% of patients undergoing hepatectomy and remains the most frequent complication after liver resection [1].

The onset of a biliary fistula is associated with the need to perform other invasive procedures, with an increase in mortality, morbidity, and hospitalization times. The improvement of instruments and techniques over the years has not led to a reduction in biliary fistulas, which, according to recent studies, are increasing along with the complexity of surgical procedures [1].

In addition to being related to infectious problems, fistulas inhibit the regenerative capacity of the liver thus influencing the prognosis of patients. The International Study Group of Liver Surgery (ISGLS) tried to give a unanimous definition and a severity grading of biliary fistulas. The definition is based on the evidence, in the drain of secretions, of a bilirubin level more than three times higher than that detected in the plasma at the same time. There are three degrees of severity: (1) *grade A,* bile loss requiring small or

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no changes in the clinical management of patients; (2) *grade B*, either a grade A bile loss lasting more than 1 week or a bile loss that requires a change in the patient's clinical management manageable without relaparotomy (e.g., additional diagnostic or interventional procedures); (3) *grade C***,** bile loss requiring invasive intervention [2].

In other words, when the fistula is low-flow it generally resolves spontaneously or with minimally invasive procedures for radiological or endoscopic detention of the biliary tract. Only in case of failure of the minimally invasive approach, a new invasive surgery can be required. The presence of bile in the peritoneal cavity, for its intrinsic quality very irritating to the tissues, represents a real threat to the patient and constitutes a possible source of severe complications, from sepsis to lesions due to erosion of anatomical structures. Therefore, prompt percutaneous drainage should be performed in the case of evidence of intra-abdominal collections.

From the beginning of the hepatic surgical experience, at least one abdominal drain was routinely placed at the end of the operation with the dual purpose of early diagnosing biliary fistula and facilitating its spontaneous resolution by avoiding the formation of abdominal collections that could easily become infected or create damage. For some years now in the literature, in the face of complications related to the drainage itself, there is unanimous agreement to place the drain only in patients who have a high risk of developing a biliary fistula.

Therefore, the goal of the study is to identify risk factors for biliary fistula. This can aid in the selection of patients in which to place a surgical drain after surgery.

Materials and methods

Data for this retrospective study were collected from June 2016 to March 2021 in the context of a research project for the Doctoral programme in *Experimental Oncology and Surgery of the University of Palermo*, in cooperation with the *Department for the Treatment and Study of Abdominal Diseases and Abdominal Transplantation* of IRCCS-ISMETT. The study enrolled all patients who underwent hepatoresective surgery for the treatment of malignant liver lesions at the Abdominal Diseases Department of IRCCS-ISMETT. Living donors and patients affected by benign lesions were then excluded from the study.

Hepatic parenchyma resections were performed using energy devices (Aquamantys, CUSA, Thunderbird, Ultracision and bipolar forceps). Intraoperative ultrasonogram was routinely used to identify lesions and define resection planes. In case of anatomic hepatectomies, a preliminary vascular check of the hilum was always performed, followed by the parenchymal transection and the section of the hepatic veins with a linear stapler. In case of minor resections (segmentectomies and wedge resections), extensive liver mobilization was always performed for better control of the surgical field. These conditions minimized the need for intermittent clamping of the hepatic hilum to control bleeding (Pringle's maneuver was performed only 10 times 2.6% of cases). Blood loss was estimated by anesthesiologists as the amount of aspirated blood during surgery.

Management of biliary fistulas

Patients with evidence of biliary fistula underwent periodic abdominal ultrasound scans to evaluate any intraperitoneal collections and daily qualitative and quantitative monitoring of the drained fluid. In presence of high-flow fistulas or infectious complications, minimally invasive endoscopic procedures (ERCP, sphincterotomy, positioning of a plastic biliary stent) or radiological procedures (positioning of ultrasound-guided pigtails to drain the infected collections or PTC with placement of external-internal biliary catheters) were performed. Figure 1 illustrates a cholangiogram that shows the presence of a biliary fistula (Fig. 1a) and the subsequent positioning of an endoscopic biliary stent (Fig. 1b) to treat the biliary fistula by reducing the pressure gradient between the biliary tree and the duodenum, to create a preferential bile flow towards the duodenum.

Whenever minimally invasive procedures failed, a second surgery was performed. All patients with infectious complications underwent blood cultures and drainage fluid cultures. These patients underwent empirical broad-spectrum antibiotic therapy, subsequently modulated according to the microbiological isolations.

Statistical analysis

The study was aimed to detect potential risk factors for fistula occurrence among a set of clinical and surgical variables. A preliminary univariate analysis was performed by investigating variables distributions, both on the full sample and stratified with respect to the presence of the fistula. Categorical variables were summarized using frequency and percentage and numeric variables using median and interquartile range (IQR). Univariate logistic regressions were performed to assess associations between the outcome (fistula occurrence) and potential predictors. A multivariable logistic regression model was fitted to find a good set of predictors of biliary fistula. Variable selection for the multivariable model was made by means of a manually performed stepwise insertion algorithm based on the Akaike Information Criterion, stopped once a best-AIC set of statistically significant variables ($p < 0.05$) was achieved. All analyses and graphics were performed using the R computing environment version 4.1.2.

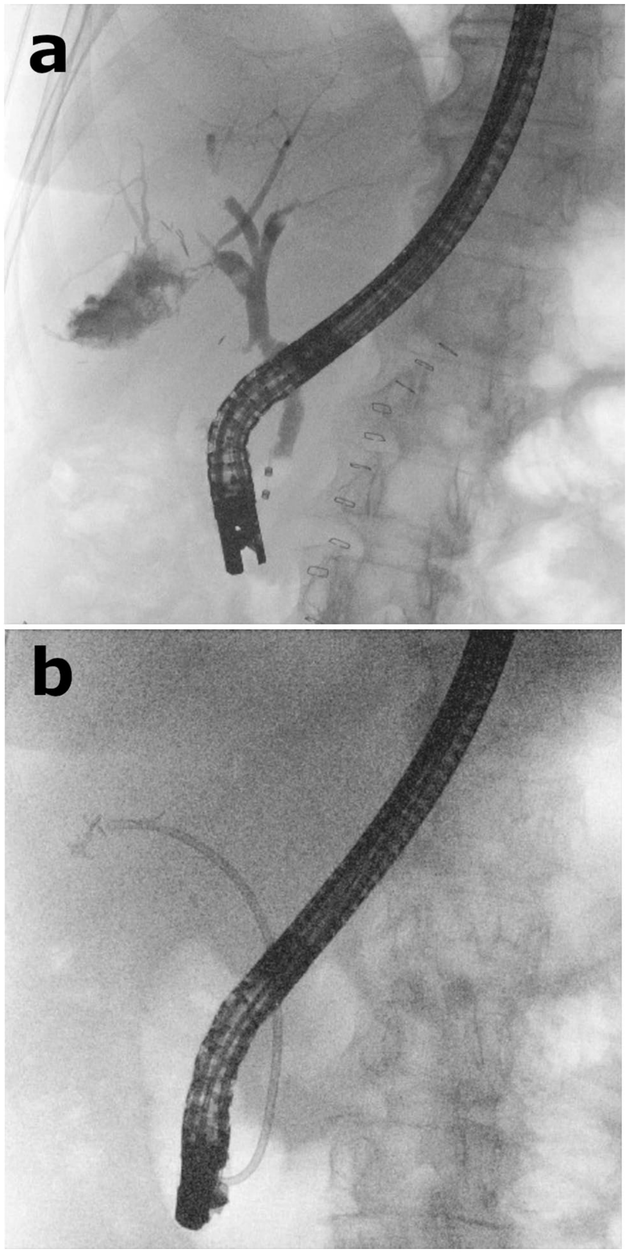

Fig. 1 Biliary fistula treatment. **a** biliary fistula detected by cholangiogram; **b** endoscopic stent placement

Results

Over the study period, 379 patients underwent a liver resection for the removal of malignant tumors and were enrolled into this study (Table 1). Two hundred and 56 (68%) were men, median age was 67 (IQR: 58–72), median body mass index (BMI) of 26 kg/m^2 (IQR: 24–28); 224 patients had primary liver tumors, in particular 176 (46%) were affected by hepatocellular carcinoma (HCC) and 48 (13%) by cholangiocarcinoma (CCA) (54% of those were intrahepatic CCAs, 13% perihilar CCAs, and 33% gallbladder tumors, respectively); 131 (35%) patients had hepatic metastases from colorectal cancer and 24 (6%) patients from primary non-colorectal liver metastases (namely, gastro-intestinal stromal tumors, neuroendocrine tumors, medullary thyroid cancers and metastases from choroid melanoma). In the group of patients with HCC, 58% had HCV-related liver disease, 11% HBV-related liver disease, 17% had nonalcoholic steatohepatitis, 8% cryptogenic cirrhosis, 5% alcohol-related liver disease.

Patients suffering from synchronous hepatic metastases from colorectal neoplasia, with primary tumor still in site, underwent liver-first approach in 85% of cases, whereas in 10% of cases were treated with combined surgery (one step resection of metastases and primary tumor), and in 5% of cases to a colon first approach for symptomaticity of the primary tumor. Neoadjuvant chemotherapy was performed in all patients with primary non-colorectal metastases, approximately 62% of patients with metachronous metastases and 48% of patients with synchronous metastases from primary colorectal neoplasms (90 patients in total, 58% of patients metastatic); recommended washout times from therapy were respected in all cases.

Fifty-two patients (14%) underwent major hepatic resection (with the removal of at least 3 liver segments), 33 (9%) of which were right hepatectomies, 17 (4%) left hepatectomies and 2 (1%) other trisegmentectomies. Sixteen patients underwent resection of the gallbladder bed after histological evidence of gallbladder cancer graded pT1b, pT2 or pT3. Overall, anatomic segmentectomies were performed on 129 (34%) patients (Table 1). Bilio-digestive anastomoses were prepared in 16 patients, 6 of which were affected by perihilar CCA and the remaining 10 by gallbladder adenocarcinoma with cystic duct infiltration; 11 patients had a percutaneous biliary catheter placed before surgery. One hundred and nine cases (29%) were performed laparoscopically; 22 were converted from laparoscopy to open surgery (conversion rate of 17%) mainly due to technical difficulties (strong adhesions, resection of posterior segments, etc.); only in two cases, conversion to open surgery was performed after a pringle maneuver did not suffice to control bleeding.

Biliary fistula actually occurred in 16 patients, half of which were classified as ISGLS grade A, 6 (38%) as grade B, and 2 as grade C. Characteristics of patients stratified for the occurrence of BL are also shown in Table 1. Specifically, the two groups are similar for patients' median ages (67, IQR: 59–72, and 62, IQR: 54–67, for patients without and with BL, respectively) and percentages of male sex patients (68% without fistula and 50% with fistula). In both groups one of the most frequent diagnoses is colorectal liver metastasis, registered respectively in 34% of patients without fistula and 44% of patients with fistula. Still, the most frequent diagnosis type in the group without fistula is HCC (47%). However, the two groups had different percentages

Table 1 Characteristics of 379 patients who underwent surgical resection for malignant diseases

	No bile leak (*N* = 363)	Bile leak (*N* = 16)	Overall (*N* = 379)
Age, years, median (IQR)	67 (59–72)	62 (54–67)	67 (58–72)
Male sex	248 (68)	8 (50)	256 (68)
Body mass index, Kg/m^2, median (IQR)	26 (24–28)	28 (24–31)	26 (24–28)
Smoke	122 (39)	4 (27)	126 (38)
Disease			
Hepatocellular carcinoma	172 (47)	4 (25)	176 (46)
Biliary cancer	44 (12)	4 (25)	48 (13)
Colorectal liver metastasis	124 (34)	7 (44)	131 (35)
Non colorectal liver metastasis	23 (6)	1 (6)	24 (6)
Cirrhosis	83 (23)	3 (19)	86 (23)
Neoadjuvant chemotherapy	104 (32)	1 (7)	105 (30)
Minimally-invasive approach	108 (30)	1 (6)	109 (29)
Anatomic resection of ≥ 3 segments	45 (12)	7 (44)	52 (14)
Biliary anastomosis	12 (3)	4 (25)	16 (4)
Concomitant procedure	24 (7)	2 (12)	26 (7)
Surgical devices			
CUSA	96 (27)	8 (50)	104 (28)
AQUAMANTYS	133 (37)	7 (44)	140 (37)
Bipolarforceps	156 (43)	5 (31)	161 (42)
Thunderbeat	117 (32)	1 (6)	118 (31)
Duration of surgery, hours, median (IQR)	3.4 (3.0–5.0)	5.0 (4.6–6.9)	4.0 (3.0–5.0)
Amine usage, n (%)	47 (13)	7 (44)	54 (14)
Estimated blood loss (cl)	25 (20–30)	40 (30–50)	25 (20–30)
Type of surgery, n (%)			
Anatomic resections	116 (32)	13 (81)	129 (34)
Right hepatectomy	31 (9)	2 (12)	33 (9)
Left hepatectomy	13 (4)	4 (25)	17 (4)
Left lobectomy	20 (6)	1 (6)	21 (6)
Other bisegmentectomy	12 (3)	2 (12)	14 (4)
Single segmentectomy	39 (11)	3 (19)	42 (11)
Other anatomic	1 (0)	1 (6)	2 (1)
Non-anatomic resections	247 (68)	3 (19)	250 (66)
Wedge (1 nodule)	172 (47)	1 (6)	173 (46)
Wedge (2 nodules)	31 (9)	1 (6)	32 (8)
Wedge (≥ 3 nodules)	28 (8)	1 (6)	29 (8)
Resection of gallbladder bed	16 (4)	0 (0)	16 (4)
ISGLS[a] biliary fistula grade, *n* (%)			
0	363 (100%)	–	363 (96%)
A	–	8 (50%)	8 (2%)
B	–	6 (38%)	6 (2%)
C	–	2 (12%)	2 (1%)

[a]*ISGLS* International study group of liver surgery

of patients having a major resection (12% of patients without fistula and 44% with fistula) and an anatomic resection (32% without fistula and 81% with fistula). The two groups were also markedly different with respect to the presence of biliary anastomosis (3% vs. 25% in patient without BL and with BL, respectively) and the administration of amines (13% vs. 44%). Bilio-digestive anastomoses was made in the two patients who subsequently developed a grade C fistula and in the second surgery, therefore, the anastomoses were repackaged. Percutaneous biliary catheters were placed in both cases prior to reoperation. Median duration of surgery was 3.4 (IQR: 3.0–5.0) hours for patients without BL and 5.0 (IQR: 4.6–6.9) hours for patients with BL, with different amounts of estimated blood loss (25 cl, IQR: 20–30, and 40 cl, IQR: 30–50, for patients without BL and with BL, respectively. Resolution of fistulas occurred in 100% of cases (0% mortality).

Univariate logistic regression models, showed significant associations of BL with BMI (OR: 1.19, 95% C.I.: 1.03–1.36, $p = 0.015$), major liver resection (OR: 5.50, 95% C.I.: 1.95–15.49, $p = 0.001$), anatomical resection (OR: 9.07, 95% C.I.: 2.54–32.46, $p < 0.001$), central liver involvement (OR: 10.09, 95% C.I.: 1.32–77.21, $p = 0.026$), presence of biliodigestive anastomosis (OR: 9.75, 95% C.I.: 2.74–34.70, $p < 0.001$), use of amines during surgery (OR: 5.20, 95% C.I.: 1.85–14.62, $p = 0.002$), duration of the surgery (OR: 1.51, 95% C.I.: 1.19–1.90, $p < 0.001$) and intraoperative blood loss(OR: 1.10, 95% C.I.: 1.05–1.14, $p < 0.001$) (Table 2).

At multivariable logistic regression (Table 3), a good predictive set of risk factors for BL occurrence were found to consist of BMI (OR: 1.21, 95% I.C.: 1.04–1.41, $p = 0.015$),anatomical resection (OR: 8.35, 95% C.I.: 2.01–34.74, $p = 0.004$), and blood loss (OR: 1.09, 95% I.C.: 1.05–1.13, $p < 0.001$).

Table 2 Univariate logistic regression models for the probability of biliary fistula

Predictors	Odds ratio (95% C.I.)	*p* value
Age, years	0.96 (0.92–1.01)	0.064
Male Sex	0.46 (0.17–1.27)	0.134
Body mass index, Kg/m^2	1.19 (1.03–1.36)	0.015
Smoke	0.58 (0.18–1.86)	0.357
DIAGNOSIS.TYPE		
HCC	1 (baseline)	–
Liver Metastasis	2.34 (0.69–7.93)	0.172
Biliary Cancer	3.91 (0.94–16.25)	0.061
Liver Cirrhosis	0.76 (0.21–2.73)	0.673
Neoadjuvant chemotherapy	0.16 (0.02–1.20)	0.074
Laparotomic resection	6.35 (0.83–48.70)	0.075
Major resection	5.50 (1.95–15.49)	0.001
Anatomic Resection	9.07 (2.54–32.46)	< 0.001
Left lobe involvement	1.93 (0.71–5.23)	0.200
Central liver involvement (at least one of S4, S5 or S8)	10.09 (1.32–77.21)	0.026
Right posterior section involvement (at least one of S6 or S7)	1.28 (0.47–3.49)	0.626
Biliodigestive Anastomosis	9.75 (2.74–34.70)	< 0.001
Concomitant procedure	2.02 (0.43–9.40)	0.371
CUSA	2.77 (1.01–7.59)	0.047
AQUAMANTYS	1.35 (0.49–3.69)	0.565
BipolarForceps	0.60 (0.21–1.77)	0.358
Thunderbeat	0.14 (0.02–1.07)	0.059
Duration of surgery, hours	1.51 (1.19–1.90)	< 0.001
Amine usage	5.20 (1.85–14.62)	0.002
Blood loss, cl	1.10 (1.05–1.14)	< 0.001

Table 3 Multivariable logistic regression model for the probability of biliary fistula

Predictor	Odds ratio (95% C.I.)	*p* value
Age	0.95 (0.89–1.01)	0.085
BMI	1.26 (1.07–1.49)	0.005
HCC	0.27 (0.06–1.30)	0.102
Anatomic resection	4.47 (0.97–20.55)	0.054
Central liver involvement (at least one of S4, S5 or S8)	18.88 (1.14–313.18)	0.040
Right posterior involvement (at least one of S6 or S7)	4.10 (1.00–16.83)	0.050
Neoadjuvant chemotherapy	0.09 (0.01–0.88)	0.039
Amine	4.53 (1.02–20.10)	0.047
Blood loss	1.08 (1.03–1.12)	< 0.001

Discussion

Advances in surgical technique together with anesthetic and technological innovations have allowed a notable development of hepatic surgery in recent years making it increasingly safe and effective.

Despite this, BL remains the most frequent and most feared complication with an incidence between 4 and 17%, according to a recent meta-analysis [1]. BL can have quite serious consequences: it reduces the regeneration of the liver parenchyma and can be associated with abdominal sepsis, prolongs hospitalization, and costs. Our study identified among risk factors for the development of BL: BMI, resection involving one of the central segments (S4, S5, S8), intraoperative blood loss, use of amines, biliodigestive anastomosis.

In recent years, many studies have evaluated the impact of body composition on the outcome of patients undergoing liver surgery. Obesity and even more so obesity-sarcopenia (a typical condition of cancer patients) are known to be related to the risk of postoperative complications [3]. Obesity, as is known, causes important metabolic and hormonal disorders with important repercussions on the liver parenchyma [4]. This condition, associated with microcirculatory disorders caused by metabolic disorders can damage the residual liver after hepatectomy and affect healing of the cut surface tissue, which may increase the risk of postoperative bile leakage [5].

The study showed a strong correlation between the type of resection performed and the onset of BL. In particular, resections involving segments 4–5–8 (called central segments) are at a higher risk of fistula. Due to their anatomical position, during the resection of the central segments, the main Glisson system around the hilum is easily damaged, thus causing bile leakage. Central hepatectomy involves a larger resection area, and no tissue coverage may also be one of the reasons for post-operative bile leakage. [5]

Notably, we also found a strong association between anatomical resection and the onset of BL. Anatomical liver resection requires a much more invasive manipulation of the Glisson ligaments, and resection of the central area of the hepatic portal region may increase the occurrence of bile leakage. This association could play an important role in the risk–benefit assessment related to anatomic resection, certainly more advantageous from a prognostic point of view, but riskier. We have insufficient evidence, and more studies are needed to verify this conjecture in the future further.

Intraoperative blood loss is also a risk factor related to the occurrence of BL. Anemization associated with clamping of the hepatic pedicle (Pringle's maneuver) is sometimes necessary to dominate massive bleeding and can cause ischemia of the liver and reperfusion injury with effects on liver function and fistula development[6].

Use of amines during surgery is a condition that underlies hypotension and hemodynamic instability often associated with blood loss or sepsis. The amines act on the microcirculation, helping to create ischemia of the liver which is correlated with a disorder of parenchyma scarring and the onset of biliary fistula. [5]

A strong association between the presence of biliary anastomosis and the onset of the fistula is well known in the literature. The use of preoperative endoscopic or percutaneous biliary drainage remains controversial. On the one hand, it facilitates the recognition of biliary structures, which can be maintained in the trans-anastomotic site to guarantee the anastomosis itself. Still, on the other, it exposes the patient to an infectious risk. Although the routine use of preoperative biliary drainage is not recommended, it has been shown that the outcome is better in selected patients (jaundice patients, cholangitis) [7, 8]

We did not find a significant association between BL and the devices used nor differences between laparoscopy and laparotomy, as is known in the literature. [9]

Another fact that emerges from our analysis is the protective role of neoadjuvant chemotherapy. Although its hepatotoxic effects are known (steatohepatitis related to irinotecan and damage to the liver sinusoids related to oxaliplatin) when respecting the recommended washout, neoadjuvant chemotherapy has proved to be a safe and effective treatment. [10]

Knowing the risk factors for the development of biliary leakage is important to prevent its appearance and possibly facilitate its spontaneous resolution. Experience has shown that most biliary fistulas resolve spontaneously. In these cases drainage plays a fundamental role because it avoids the formation of abdominal collections that can easily become infected and cause sepsis. However, the routine usage of abdominal drainage at the end of liver resection is controversial [11, 12]. On the one hand, drainage allows for early detection of any complications such bleeding and biliary fistula; on the other hand it is itself a procedure prone to the onset of other complications such as increased ascitic production, retrograde infections, pain, intestinal injuries, increased costs, slowing of rehabilitation of the patient and prolongation of hospitalization [13]. In the literature, there is therefore a wide consensus on discouraging routine usage of drainage after surgery, but to reserve its placement only for selected patients, who indeed are at greater risk to develop BL. [14]

This study has some limitations. Even if the sample size is not exceedingly small, the distribution of patients with respect to the event of interest is severely unbalanced, with only 16 patients who experienced BL. This, together with the retrospective nature of the study which did not allow a proper a-priori stratification with respect to some important factors (biliary cancer vs. other tumors, cirrhotic vs. non cirrhotic liver, anatomic vs. non-anatomic resection, etc.), limited the possibility of studying the correlational structure of the variables, possibly hid important predictors of BL due internal correlation among variables, and almost certainly inflated confidence intervals' sizes. In addition, we lacked information on a number of variables that are part of already proposed useful risk scores (see for example[15] and the Vasoactive-inotropic score[16]).

Conclusions

Resections involving the central segments (S4-5–8), biliodigestive anastomosis, intraoperative use of the amine, BMI and blood loss are risk factors for the development of BL. Identifying this risk factors can guide the choice of positioning a drain at the end of the liver resection.

Authors' contributions Conceptualization, SC and SG: validation, SC and DP: formal analysis, MB: resources, SLP: data curation, SC: writing—original draft preparation, SC: writing—review and editing, MB, NG, CC, GP, SLP: supervision, SG. All authors have read and agreed to the published version of the manuscript.

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Availability of data and materials The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Conflicts of interest The authors have no relevant financial or non-financial interests to disclose.

Institutional review board statement The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Research Review Board of ISMETT (protocol code IRRB/31/09).

Informed consent statement Informed consent was obtained from all patients involved in the study.

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References

1. Yang T, Li L, Zhong Q, Lau WY, Zhang H, Huang X, Yu WF, Shen F, Li JW, Wu MC (2013) Risk factors of hospital mortality after re-laparotomy for post-hepatectomy hemorrhage. World J Surg 37:2394–2401
2. Koch M, Garden OJ, Padbury R, Rahbari NN, Adam R, Capussotti L, Fan ST, Yokoyama Y, Crawford M, Makuuchi M, Christophi C, Banting S, Brooke-Smith M, Usatoff V, Nagino M, Maddern G, Hugh TJ, Vauthey JN, Greig P, Rees M, Nimura Y, Figueras J, DeMatteo RP, Büchler MW, Weitz J (2011) Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International study group of liver surgery. Surgery 149(5):680–688. https://doi.org/10.1016/j.surg.2010.12.002
3. Lodewick TM, van Nijnatten TJ, van Dam RM et al (2015) Are sarcopenia, obesity and sarcopenic obesity predictive of outcome in patients with colorectal liver metastases? HPB (Oxford) 17(5):438–446
4. Peng PD, van Vledder MG, Tsai S et al (2011) Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. HPB (Oxford) 13(7):439–446
5. Tan L, Liu F, Liu Z-L, Xiao J-W (2021) Meta-analysis of risk factors for bile leakage after hepatectomy without biliary reconstruction. Front Surg. 8:764211
6. Gruttadauria S, SaintGeorges Chaumet M, Pagano D, Marsh JW, Bartoccelli C, Cintorino D, Arcadipane A, Vizzini G, Spada M, Gridelli B (2011) Impact of blood transfusion on early outcome of liver resection for colorectal hepatic metastases. J Surg Oncol 103:140–147. https://doi.org/10.1002/jso.21796
7. Cillo U, Fondevila C, Donadon M, Gringeri E, Mocchegiani F, Schlitt HJ, Ijzermans JNM, Vivarelli M, Zieniewicz K, Olde Damink SWM, Koerkamp G (2019) Surgery for cholangiocarcinoma. B Liver Int. https://doi.org/10.1111/liv.14089
8. She WH, Cheung TT, Ma KW, Yin Tsang SH, Dai WC, Yan Chan AC (2021) Lo Impact of preoperative biliary drainage on postoperative outcomes in hilar cholangioca cinoma CM. Asian J Surg 26:S1015-9584
9. Yoh T, Cauchy F (2022) Soubrane O—oncological resection for liver malignancies: can the laparoscopic approach provide benefits? Ann Surg 275(1):182–188
10. Wiseman JT, Guzman-Pruneda F, Xourafas D, Chun YS, Ejaz A, Tsung A, Pawlik TM, Jordan M (2019) Cloyd—impact of neoadjuvant chemotherapy on the postoperative outcomes of patients undergoing liver resection for colorectal liver metastases: a population-based propensity-matched analysis. J Am Coll Surg 229(1):69–77
11. Wada S, Hatano E, Yoh T, Seo S, Taura K, Yasuchika K, Okajima H, Kaido T (2017) Uemoto Is routine abdominal drainage necessary after liver resection? S Surg Today 47(6):712–717. https://doi.org/10.1007/s00595-016-1432-3 (**Epub 2016 Oct 24**)
12. Donadon M, Costa G, Cimino M, Procopio F, Del Fabbro D, Palmisano A (2016) Torzilli diagnosis and management of bile leaks after hepatectomy: results of a prospective analysis of 475 hepatectomies G. World J Surg 40(1):172–181
13. Anweier N, Apaer S, Zeng Q, Wu J, Gu S, Li T (2021) Zhao J - Is routine abdominal drainage necessary for patients undergoing elective hepatectomy? A protocol for systematic review and meta-analysis. Tuxun T Medicine (Baltimore) 100(6):e24689
14. Gavriilidis P, Hidalgo E, de Angelis N, Lodge P, Azoulay D (2017) Re-appraisal of prophylactic drainage in uncomplicated liver resections: a systematic review and meta-analysis. HPB 19(1):16–20. https://doi.org/10.1016/j.hpb.2016.07.010 (**Epub 2016 Aug 26**)
15. Mohkam K, Farges O, Vibert E, Soubrane O, Adam R, Pruvot FR, Regimbeau JM, Adham M, Boleslawski E, Mabrut JY (2018) Association de Chirurgie Hépato-Biliaire et de Transplantation (ACHBT) French Hepatectomy Study Group. Risk score to predict biliary leakage after elective liver resection. Br J Surg 105(1):128–139. https://doi.org/10.1002/bjs.10647
16. Lai Q, Ghinolfi D, Avolio AW, Manzia TM, Mennini G, Melandro F, Frongillo F, Pellicciaro M, Larghi Laureiro Z, Aglietti R, Franco A, Quaranta C, Tisone G, Agnes S, Rossi M, de Simone P (2022) Proposal and validation of a liver graft discard score for liver transplantation from deceased donors: a multicenter Italian study. Updates Surg. 74(2):491–500. https://doi.org/10.1007/s13304-022-01262-0 (**Epub 2022 Mar 11. PMID: 35275380; PMCID: PMC8995238**)