

Predictors of the Effectiveness of Prophylactic Drains After Hepatic Resection

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Abstract

Background Randomized clinical trials have demonstrated the limited efficacy of prophylactic drains following hepatic resection. However, many surgeons still insist on using prophylactic drains. This study was designed to identify patients who require prophylactic drains to manage or monitor postoperative complications after hepatic resection.

Methods Data were retrospectively collected from 316 patients who underwent hepatic resection and received a prophylactic drain. The patients were divided into two groups according to whether the drain was used to manage or monitor the following postoperative complications: bile leakage (prophylactic drains were used to monitor and treat bile leakage) and postoperative hemorrhage (the drainage fluid was macroscopically bloody and required drain fluid blood counts and monitoring to assess the need for transfusion or reoperation). The results were then validated in a separate cohort of 101 patients.

Results In 25/316 patients (7.9 %), the prophylactic drains were clinically effective, being used to manage bile leakage in 18 patients and hemorrhage in 8. Intraoperative bile leakage ($P = 0.021$) and long operation time (≥ 360 min) ($P = 0.017$) were independent predictors of bile leakage. Intraoperative blood loss (≥ 650 ml) ($P = 0.0009$) was an independent predictor of hemorrhage. In the subsequent 101 patients, prophylactic drains were clinically effective in patients with one of these predictors with sensitivity, specificity, and false-negative rates of 88.9, 62.0, and 1.7 %, respectively.

Conclusion A prophylactic drain should be considered following hepatic resection for patients with intraoperative bile leakage, operation time of ≥ 360 min, or blood loss of ≥ 650 ml.

Introduction

Because of recent advances in surgical techniques, hepatic resection is being performed with increasing frequency, and the mortality and morbidity rates are steadily

decreasing [1, 2]. Several recent randomized clinical trials (RCTs) have revealed that prophylactic drains are unnecessary after elective liver resection [3, 4]. Moreover, prophylactic drains may increase the risk of surgical site infection (SSI) [3, 5]. Nevertheless, many surgeons

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continue to insert prophylactic drains because they are thought to facilitate early detection and treatment of complications such as bile leakage or hemorrhage [6, 7].

Considering that the effectiveness of prophylactic drains may depend on the individual patient's characteristics, it may be prudent to limit their use to patients who are likely to benefit in terms of the management and treatment of postoperative complications. Some reports have proposed criteria for early drain removal based on the drainage fluid bilirubin level and fluid volume measured on postoperative day (POD) 3 [5, 7]. Other studies have revealed risk factors for additional postoperative procedures based on the hepatectomy method, intraoperative bile leakage, and intraoperative blood loss [8, 9]. To our knowledge, however, no prior studies have attempted to identify criteria for using prophylactic drains in individual patients. Therefore, the aim of the present study was to identify possible clinical predictors of effective use of a prophylactic drain to detect and manage postoperative complications following hepatic resection.

Patients and methods

Patients

Two analyses were conducted in this study. The first analysis retrospectively assessed the characteristics of 370 patients whose prophylactic drains were clinically effective in the short-term postoperative period after elective hepatic resection, including 69 laparoscopic resections, at the Department of Surgery and Science, Kyushu University Hospital from January 2009 to December 2013. Forty-eight patients who underwent concomitant procedures on other organs, including bile duct reconstruction or gastrointestinal resection, were excluded from this study. Overall, 316/322 patients (98.1 %) received prophylactic drains and were enrolled in this study. The reasons for hepatic resection in these 316 patients included hepatocellular carcinoma ($n = 212$, 67 %), other liver carcinomas ($n = 27$, 9 %), liver metastases ($n = 60$, 19 %), benign tumors ($n = 11$, 3 %), and liver cysts ($n = 6$, 2 %). The operative procedures were as follows: lobectomy ($n = 45$, 14 %) or resection of more than one segment ($n = 6$, 2 %), segmentectomy ($n = 60$, 19 %), subsegmentectomy ($n = 47$, 15 %), and partial hepatectomy ($n = 158$, 50 %). One prophylactic drain was routinely inserted near the cut surface of the liver at the end of surgery. The second analysis was performed to validate the reliability of the results obtained from the first analysis and included data from a separate cohort of 101 patients who underwent hepatic resection from January 2014 to March 2015.

Study design

We divided the 316 patients into 2 groups according to whether the drain was used to manage or monitor postoperative complications. Predictors of the effectiveness of prophylactic drains were identified using multivariate analysis of clinical factors. The accuracy of the identified predictors was assessed in the subsequent cohort of 101 patients.

Surgical procedures and patient management

Patients were carefully selected for major hepatic resection based on volumetric analysis of the remnant liver to prevent postoperative liver failure [10–12]. The type of hepatic resection was determined according to the preoperative indocyanine green (ICG) retention rate at 15 min [13]. Parenchymal dissection of the liver was performed using a Cavitron Ultrasonic Surgical Aspirator system (CUSA system, Valleylab Inc., Boulder, CO, USA) and a VIO system (VIO 300D; ERBE Elektromedizin, Tübingen, Germany) containing a soft-coagulation mode tip (SOFT COAG) and a bipolar clamp (BiClamp) for laparoscopic resection [14, 15]. Intraoperative blood flow control was achieved with the Pringle maneuver (15-min occlusion and 5-min release). Possible bile leakage was tested using ICG solution whenever possible [16] ($n = 121$, 38.3 %). We defined intraoperative bile leakage as a positive intraoperative bile leakage test result or the presence of bile on the cut surface of the liver during surgery. If bile leakage was detected, the leakage point was repaired by Z-sutures using 6–0 polydioxanone (PDSII; Johnson & Johnson, Tokyo, Japan). An absorbable polyglactin acid sheet mesh (Neoveil, Gunze, Tokyo, Japan) and fibrin glue (Bolheal; Kaketsuken, Kumamoto, Japan or Beriplast; Nycomed, Zurich, Switzerland) were routinely applied to the cut surface of the liver. Anticoagulant drugs, such as nafamostat mesilate [17], were administered perioperatively to prevent postoperative disseminated intravascular coagulation. The patients were also preoperatively administered 500 mg of methylprednisolone [18].

Drain insertion and management

A 15-Fr closed suction drain (J-Vac drain; Johnson & Johnson, Somerville, NJ, USA) was inserted near the cut surface of the liver at the end of surgery. Fluid was aspirated from the drain daily to measure the total bilirubin concentration [19]. The prophylactic drains were usually removed by POD 3 unless the drainage fluid was grossly bloody, exceeded 100 ml/day, or did not meet the bile leakage criteria of the International Study Group of Liver Surgery (ISGLS) [19]. In these cases, the drainage tube was retained until the fluid turned clear, bile leakage

Table 1 Predictors of the effectiveness of prophylactic drains for the management of bile leakage

Variables	Patients with an ineffective drain (<i>n</i> = 298)	Patients with an effective drain (<i>n</i> = 18)	<i>P</i> value (univariate analysis)	<i>P</i> value (multivariate analysis)
Age (years)	66 ± 0.67	65 ± 2.76	0.858	
Males/females	206/92	14/4	0.455	
BMI (kg/cm ²)	22.9 ± 0.19	24.7 ± 0.79	0.030	0.076
DM	65 (21.8 %)	2 (11.1 %)	0.281	
Child–Pugh B	6 (2.0 %)	0 (0 %)	0.543	
Liver damage B	42 (14.1 %)	1 (5.6 %)	0.305	
T-bil (mg/dl)	0.78 ± 0.02	0.76 ± 0.09	0.743	
Albumin (g/dl)	3.98 ± 0.03	4.06 ± 0.11	0.536	
PT (%)	94.29 ± 0.83	97.0 ± 3.21	0.591	
Laparoscopic resection	67 (22.5 %)	2 (11.1 %)	0.381	
Operation time (min)	317 ± 6.9	419 ± 28	0.0005	0.021
Blood loss (ml)	507 ± 37	1043 ± 151	0.083	
Blood transfusion	35 (11.7 %)	4 (23.5 %)	0.189	
Pringle maneuver (min)	49 ± 3	50 ± 11	0.921	
Intraoperative bile leakage	60 (20.1 %)	10 (55.6 %)	0.0004	0.017
Maximum tumor diameter (cm)	1.0 ± 0.1	1.8 ± 8 1	0.095	
Volume of resected liver (g)	416 ± 130	306 ± 552	0.847	
HCC	25 (67.8 %)	10 (55.6 %)	0.284	
HLC (F3/F4)	89 (30.0 %)	5 (27.8 %)	0.839	

Bold values are statistically significant ($P < 0.05$)

Values are presented as the *n* (%) or mean ± standard deviation

BMI body mass index, *DM* diabetes mellitus, *T-bil* total bilirubin, *PT* prothrombin time, *HCC* hepatocellular carcinoma, *HLC* histological liver cirrhosis

disappeared [19], or the drainage volume decreased to <100 ml/day. If the drainage fluid volume of serous ascites was the only reason to retain the drainage tube, the wound around the drain site was sutured after drain removal.

Definitions of clinical effectiveness of prophylactic drains

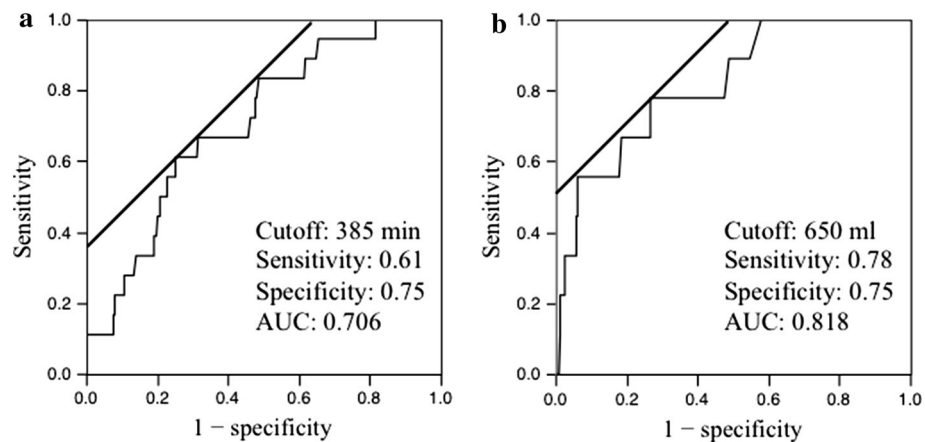
A prophylactic drain was considered clinically effective if the drainage fluid color or volume contributed to the guidance or treatment of the following postoperative complications: bile leakage ($n = 18$) or postoperative hemorrhage ($n = 8$). Routine abdominal X-rays were obtained just after the operation and the next day to avoid dislocation of the prophylactic drains; therefore, we consider that all prophylactic drains actually worked to monitor the postoperative complications. For bile leakage, the prophylactic drain was deemed effective if it was used to monitor the severity of bile leakage. Bile leakage was defined according to the criteria of the ISGLS as a drain fluid-to-serum total bilirubin concentration ratio of ≥ 3.0 on or after POD 3. Beyond POD 3, we continued to monitor the drain if the bilirubin ratio remained ≥ 3.0 . Postoperative hemorrhage was defined as drainage fluid that was macroscopically bloody and required multiple

blood tests or a drainage fluid blood count to check for progressive anemia. The severity of postoperative hemorrhage was monitored to assess the need for transfusion or reoperation.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation. In univariate analyses, continuous variables were compared using Student's *t* test and categorical variables were compared using the χ^2 test or Fisher's exact test. Variables with a *P* value of <0.05 in the univariate analysis were included in a stepwise logistic regression analysis to identify independent predictors of bile leakage and postoperative hemorrhage. In all analyses, $P < 0.05$ was considered statistically significant. Estimation of the cutoff values of operation time and intraoperative blood loss for predicting bile leakage and postoperative hemorrhage, respectively, was performed by calculating the areas under the receiver operating characteristic (ROC) curves. The ROC curve is a plot of sensitivity versus 1—specificity for all possible cutoff values. The optimal cutoff values used were selected based on the sensitivity, specificity, positive predictive value, and negative predictive value. All analyses were performed using JMP Version 9.0.2 (SAS Institute, Inc., Cary, NC, USA).

Fig. 1 a Receiver operating characteristic curves using operation time as a predictor of the effectiveness of prophylactic drains in the management of bile leakage. **b** Receiver operating characteristic curves using operation time as a predictor of the effectiveness of prophylactic drains in the management of postoperative hemorrhage. AUC area under the curve



Results

Characteristics of patients with clinically effective prophylactic drains

The patients were divided into two groups: patients whose drain was clinically effective ($n = 25$, 7.9 %) and patients whose drain was not clinically effective ($n = 291$, 92.1 %). In one patient, the drain was effective in terms of detecting early postoperative hemorrhage from POD 0 to POD 1 and bile leakage from POD 8 to POD 31. Therefore, the drains were effective in 26 patients (bile leakage in 18 patients and postoperative hemorrhage in 8 patients). Ten patients with bile leakage needed no additional radiological or surgical intervention. Additional treatment with endoscopic retrograde cholangiopancreatography, exchange of the drainage tube, establishment of secondary percutaneous drainage, and surgery were performed in three, three, one, and one patient, respectively. Of the eight patients with postoperative hemorrhage, five were managed with fresh frozen plasma; one of these five required relaparotomy.

Predictors of the effectiveness of prophylactic drains for managing bile leakage

Clinical factors related to the effectiveness of prophylactic drains for managing bile leakage, including patient characteristics, surgical factors, and tumor-related factors, were compared between the patients without and with effective drains (Table 1). In the univariate analyses, patients without and with effective drains exhibited statistically significant differences in body mass index (22.9 vs. 24.7 kg/m², respectively; $P = 0.030$), operation time (317 vs. 419 min, respectively; $P = 0.0005$), and intraoperative bile leakage (20.1 vs. 55.6 %, respectively; $P = 0.0004$). Multivariate logistic regression revealed that operation time ($P = 0.021$) and intraoperative bile leakage ($P = 0.017$)

were significantly associated with the effectiveness of prophylactic drains for managing bile leakage. Figure 1a shows the ROC curve of operation time. The optimal cutoff value was 385 min (sensitivity, 0.61; specificity, 0.75). Similar sensitivity and specificity values (0.67 and 0.68, respectively) were obtained when we used a cutoff value of 360 min, which is simpler in clinical use. Therefore, we defined the cutoff value of operation time as 360 min for predicting the effectiveness of prophylactic drains.

Predictors of the effectiveness of prophylactic drains for managing postoperative hemorrhage

In the univariate analyses to identify factors related to the effectiveness of prophylactic drains for managing postoperative hemorrhage, patients without and with effective prophylactic drains exhibited significant differences in operation time (321 vs. 429 min, respectively; $P = 0.018$), intraoperative blood loss (511 vs. 1560 ml, respectively; $P < 0.001$), intraoperative blood transfusion (11.8 vs. 33.3 %, respectively; $P = 0.028$), and the duration of the Pringle maneuver (48 vs. 85 min, respectively; $P = 0.021$) (Table 2). In the multivariate analysis, the only independent predictor was intraoperative blood loss ($P = 0.008$). Figure 1b shows the ROC curve of blood loss. Because the optimal cutoff value for blood loss was 650 ml (sensitivity, 0.78; specificity, 0.75), we used this as the cutoff value for predicting the effectiveness of prophylactic drains.

Validation of the predictors of the effectiveness of prophylactic drains

The predictors of the effectiveness of prophylactic drains (intraoperative bile leakage, operation time of ≥ 360 min, and blood loss of ≥ 650 ml) were validated in the second analysis using a separate cohort of 101 patients. The sensitivity was 88.9 %, and the specificity was 62.0 %. Of 58

Table 2 Predictors of the effectiveness of prophylactic drains for the management of postoperative hemorrhage

Variables	Patients with an ineffective drain (<i>n</i> = 308)	Patients with an effective drain (<i>n</i> = 8)	<i>P</i> value (univariate analysis)	<i>P</i> value (multivariate analysis)
Age (years)	66 ± 0.66	61 ± 4.13	0.252	
Males/females	215/93	6/2	0.752	
BMI (kg/cm ²)	23.0 ± 0.19	24.5 ± 1.19	0.201	
DM	67 (21.8 %)	0 (0 %)	0.137	
Child–Pugh B	6 (2.0 %)	0 (0 %)	0.690	
Liver damage B	43 (14 %)	0 (0 %)	0.256	
T-bil (mg/dl)	0.79 ± 0.02	0.60 ± 0.13	0.165	
Albumin (g/dl)	3.99 ± 0.03	4.00 ± 0.17	0.968	
PT (%)	91.7 ± 0.82	93.6 ± 5.08	0.707	
Laparoscopic resection	68 (22.1 %)	1 (12.5 %)	0.517	
Operation time (min)	321 ± 7	429 ± 42	0.013	0.744
Blood loss (ml)	511 ± 36	1560 ± 223	<0.0001	0.008
Blood transfusion	36 (11.7 %)	3 (33.3 %)	0.028	0.884
Pringle maneuver (min)	48 ± 3	85 ± 16	0.021	0.226
Intraoperative bile leakage	67 (21.8)	3 (37.5 %)	0.290	
Maximum tumor diameter (cm)	1.06 ± 0.11	1.17 ± 0.74	0.884	
Volume of resected liver (g)	417 ± 128	168 ± 808	0.762	
HCC	207 (67.2 %)	5 (62.5 %)	0.780	
HLC (F3/F4)	91 (30.0 %)	2 (25.0 %)	0.759	

Bold values are statistically significant ($P < 0.05$)

Values are presented as the *n* (%) or mean ± standard deviation

BMI body mass index, *DM* diabetes mellitus, *T-bil* total bilirubin, *PT* prothrombin time, *HCC* hepatocellular carcinoma, *HLC* histological liver cirrhosis

patients who had none of these predictors, 1 (1.7 %) had a clinically effective prophylactic drain resulting in a negative predictive value of 98.3 %. Of 43 patients with any of these predictors, 8 (18.6 %) had clinically effective prophylactic drains, resulting in a positive predictive value of 18.6 %. Therefore, the accuracy of our predictors was 64.4 %.

Discussion

The present study showed that prophylactic drains were effective in 25 patients (7.9 %, 26 cases), including 18 patients with bile leakage (5.7 %) and 8 patients with postoperative hemorrhage (2.5 %), similar to the results of other studies [6, 7]. Refractory ascites is another important problem after hepatic resection, but in this study we focused more on the early effectiveness, not long-term effectiveness. When we analyzed predictors of the effectiveness of prophylactic drains for refractory ascites, independent factors were a low serum albumin level (<3.9 mg/dl) ($P = 0.010$) and long operation time (≥ 360 min) ($P = 0.023$), the latter of which is also one of our criteria.

Less than half of the patients (43/101) met our predictors of prophylactic drain insertion. The others had none of the predictors, and we could have skipped inserting a

prophylactic drain in these patients. Notably, our predictors of effective prophylactic drain insertion included all of the patients with major complications ($n = 5$, 5.0 %) of Clavien grade IIIa or greater [20], which suggests that these predictors should allow us to identify patients who require drain insertion for safety concerns.

Several reports have proposed criteria for selective drain placement based on the need for additional postoperative interventions [8, 9]. Our criteria differ from theirs because we evaluated prophylactic drains not only as therapeutic tools, but also as diagnostic tools. Hirokawa et al. [8] reported the following predictors of effective prophylactic drain insertion: extended hepatic resection with portal vein thrombus, use of a high-risk hepatectomy procedure (e.g., central bisegmentectomy or anterior segmentectomy exposing the major Glisson's sheath), repeated hepatic resection, and intraoperative bile leakage. When we applied these criteria to our 101 patients in the second analysis of the present study, the sensitivity was 66.7 % (6/9) and the specificity was 50.0 % (46/92). Sensitivity was lower than our criteria (88.9 %), which could induce omitting patients who should have prophylactic drains. Ishizawa et al. [9]. Reported the following criteria for prophylactic drain insertion: blood loss of >400 ml, preoperative chemotherapy, intraoperative bile leakage, bilioenteric anastomosis,

and increased risk of postoperative bleeding. When we applied these criteria to our 101 patients in the second analysis, the sensitivity was 88.9 % (8/9) and the specificity was 38.0 % (35/92). These criteria only applied to 35.6 % of the patients (35/101) to the no-drain group. Because Ishizawa et al. [9] focused on laparoscopic hepatic resection, the criteria might not be appropriate for patients undergoing other surgical procedures.

In our series, postoperative complications classified as Clavien grade II or greater occurred in 28.6 % of patients (90/316), and reoperation was necessary in 0.9 % of patients (3/316). In the present study, there were no in-hospital mortalities. In earlier studies with a no-drain policy after hepatic resection, reoperation was necessary in 1.9 % of patients (1/52 cases) [21] and the in-hospital mortality rate was 1.7 % (1/60) in one study [21] and 1.9 % (1/52) in another study [3]. Prophylactic drains could have allowed the early detection and treatment of postoperative complications, prevented in-hospital mortality, and reduced the need for reoperation. By contrast, the rate of complications in patients with a prophylactic drain was similar to that in patients without prophylactic drains (28.6 %) in another study [8]. SSI, which were defined using standardized surveillance criteria [22], occurred in 11.4 % of patients (36/316), which is similar to the rate in patients with no drains (13.5 %) [21]. Prophylactic drains can be safely placed without increasing the risk of SSI through optimal drain management [7].

Although numerous studies have recommended a no-drain policy [3, 8, 9, 21], several patients in our series benefited from a prophylactic drain without requiring additional invasive procedures. Selective placement of a drain to manage or prevent postoperative complications in high-risk patients appears to be reasonable, and the criteria outlined in our study should help surgeons to select patients likely to benefit from a prophylactic drain.

The main limitation of this study is the retrospective data collection and analysis. Additional reports from other centers are necessary to help generalize our findings. Our criteria should play an important role in helping future RCTs to elucidate the clinical role of prophylactic drains in a relatively safe manner.

In conclusion, prophylactic drain insertion after hepatic resection is clinically effective in terms of the management of bile leakage and postoperative hemorrhage. Predictors of effective prophylactic drains were the presence of intraoperative bile leakage, operation time of ≥ 360 min, and blood loss of ≥ 650 ml.

Conflict of interest The authors declare that they have no conflicts of interest or financial support.

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