Late-onset bile leakage after hepatic resection

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Background. *Postoperative bile leakage can be a serious complication after hepatic resection. Few studies have analyzed patients according to the time of onset of bile leakage. We analyzed differences between patients with early- and late-onset bile leakage after hepatic resection and assessed clinical characteristics and outcomes in patients with late-onset leakage.*

Methods. *Between 2008 and 2010, 1,009 patients underwent hepatic resection at 4 participating university hospitals and 2 community hospitals. Fifty-two patients (5.1%) with postoperative bile leakage were divided into an early-onset group (<2 weeks after surgery,* n = *34) and a late-onset group (≥2 weeks after surgery,* n = *18). Patient characteristics and outcomes were collected prospectively and analyzed retrospectively.*

Results. *The proportion of patients who underwent intra-abdominal placement of a drainage catheter was significantly less in the late-onset group than the early-onset group. All 18 patients in the late-onset group developed intra-abdominal infection, and 2 died of sepsis. The proportion of patients who underwent invasive treatment (abdominal paracentesis, endoscopic biliary drainage, or second hepatic resection) was significantly greater in the late-onset group than in the early-onset group. The time to resolution of bile leakage was significantly greater in the late-onset group than the early-onset group.*

Conclusion. *Patients should be monitored carefully for bile leakage for several weeks after hepatic resection, because late-onset bile leakage can cause serious complications. Intra-abdominal infection should also be treated as soon as possible, because it may induce refractory bile leakage with serious complications.*
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Recent improvements in operative techniques of hepatic resection and perioperative care have increased the safety of hepatic operations and decreased the perioperative mortality rate.[1-4] Although the overall rate of postoperative complications has decreased, the reported rate of postoperative bile leakage remains unchanged, ranging from 3.6–33%,[5-13] making it among the most common complications after hepatic resection. Various procedures have been introduced to decrease the occurrence of bile leakage, including intraoperative testing for bile leak,[14] intraoperative cholangiography,[15] and application of fibrin glue to the cut surface of the liver.[16] Bile leakage is associated with sepsis, liver failure, postoperative mortality, and a greater duration of hospital stay.[6] Understanding the pathophysiology of bile leakage may minimize its occurrence and prevent serious complications.

Several studies have focused on identifying risk factors for postoperative bile leakage after hepatic resection.[17-19] Although a number of risk factors have been identified, the reported importance of these factors varies among studies. Few studies have analyzed patients according to the time of onset of bile leakage after hepatic resection. The aim of this study was to analyze differences between patients with early- and late-onset bile leakage after hepatic resection to assess the pathophysiology and treatment of late-onset bile leakage.

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METHODS

Subjects. Between 2008 and 2010, 1,009 patients underwent hepatic resection at 4 participating

university hospitals and 2 community hospitals. Fifty-two patients (5.1%) with postoperative bile leakage were included in this study. Postoperative bile leakage was diagnosed when there was bile leaking from the wound or the drain (total bilirubin level in the drainage fluid >3 times the serum total bilirubin level), intra-abdominal accumulation of bile confirmed by drainage, or demonstration of bile leakage on postoperative cholangiography, for >3 days.[20] Bile leakage was defined as early onset if it occurred during the first 13 postoperative days (PODs), and late onset if it occurred from POD 14, because the mean postoperative hospital stay in patients without postoperative complications was 12–13 days. The 52 patients were divided into an early-onset group (n = 34) and a late-onset group (n = 18).

Before operation, each patient underwent conventional liver function tests and measurement of the indocyanine green retention rate at 15 minutes. Patients were screened for hepatitis virus infection by measurement of hepatitis B virus surface antigen and anti-hepatitis C virus antibody.

Operative procedures. Operative procedures were classified according to the Brisbane terminology proposed by Strasberg et al.[21] Anatomic resection was defined as resection of the tumor together with the related portal vein branches and corresponding hepatic artery territory. Anatomic resection was classified as hemihepatectomy, extended hemihepatectomy, sectionectomy (resection of 2 Couinaud subsegments[22]), or segmentectomy (resection of one Couinaud subsegment). All nonanatomic resections were classified as limited resection, which were performed in patients with central or peripheral tumors and moderate liver dysfunction.[23] The Cavitron ultrasonic surgical aspirator dissector (Valleylab, Boulder, CO) was used to transect the hepatic parenchyma. Intraoperative cholangiography, bile leakage tests, and placement of drainage catheters were performed according to the policy of each hospital. Intra-abdominal drainage catheters were placed routinely after hepatectomy at 4 of the 6 hospitals. The drainage catheter was removed when the drainage fluid was minimal and not bile stained.

Clinical characteristics of patients with bile leakage. Clinical characteristics were compared between the early- and late-onset groups. The characteristics were grouped as patient-related factors, intraoperative factors, and postoperative factors. Patient-related factors included sex, age, hepatitis virus infection status, body mass index, comorbidities, liver function test results, and diagnosis. Intraoperative factors included the operative procedure, operative approach, extent of hepatic resection, concomitant cholecystectomy, method of parenchymal dissection, use of absorbable sutures, use of the Pringle maneuver during parenchymal dissection, use of fibrin glue, performance of a bile leakage test, transcystic placement of a bile duct drain, placement of an intra-abdominal drainage catheter, and period of prophylactic antibiotics. Postoperative factors included the diagnostic method and treatments for bile leakage, postoperative complications, mortality, administration of therapeutic antibiotics, and pathogens grown from infected bile.

Statistical analysis. Continuous variables are presented as median values (range). The significance of differences between the early- and late-onset groups was assessed using the Chi-square or Mann-Whitney U test as appropriate. Adjusted odds ratios (ORs) with 95% CIs for late-onset bile leakage were calculated by multivariate logistic regression analysis that included all factors found to be significantly different between the early- and late-onset groups on univariate analysis.

RESULTS

Preoperative clinical characteristics. Table I shows the preoperative characteristics of patients in the early- and late-onset groups. There were no differences between the 2 groups in sex, age, hepatitis virus infection status, body mass index, diabetes mellitus, liver cirrhosis, gallbladder disease, prothrombin time, platelet count, or serum concentrations of total bilirubin, albumin, aspartate aminotransferase, and alanine aminotransferase. The late-onset group had a lesser indocyanine green retention rate at 15 minutes and a greater proportion of patients with metastatic liver tumors than the early-onset group.

Intra- and postoperative characteristics. The operative procedure performed, operative approach, extent of hepatic resection, concomitant cholecystectomy, use of absorbable sutures, use of the Pringle maneuver during parenchymal dissection, performance of a bile leakage test, and intraoperative detection of major bile leakage did not differ significantly between the 2 groups (Table II). The proportion of patients who underwent parenchymal dissection using the Cavitron ultrasonic surgical aspirator dissector with the VIO soft coagulation system[24] was greater in the late-onset group than in the early-onset group (P = .027). The proportion of patients who underwent placement of an intra-abdominal drain was less in the late-onset group than in the early-onset group (P = .0007). The proportions of patients who underwent application of fibrin glue to the