Long-Term Changes in Hepatobiliary Physiology After Roux-en-Y Hepaticojejunostomy

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Hepaticojejunostomy (HJ) is a common operation used to by-pass extrahepatic biliary obstructions and to establish biliary-enteric continuity after resections for benign and malignant diseases. Little is known about the effect of this procedure on hepatobiliary physiology. The aim of the present study was to investigate in a swine model the changes in biliary dynamics, bile composition, and hepatic histology induced by Roux-Y HJ. Twenty-four swine (57 (47 to 76) kg) underwent cholecystectomy, with HJ (Group I; n = 12) or without any biliodigestive anastomosis (Group II, n = 12), and were followed up for 6 or 12 mo by repeated weight scaling, blood, serum, and bile analysis, 99mTc, diethyliminodiacetic acid (HIDA) dynamic biligraphy, and histological analysis. During follow-up, HJ was associated with less weight gain, colonization of the bile duct with aerobic bacteria Escherichia coli dominating (in 75% of the animals), a shortened hilum-intestine transit time but reduced liver clearance in dynamic biligraphy, and fibrous periportal changes in liver histology (in 50% of the animals). We conclude that during 1 y follow-up HJ with no anastomotic stricture formation is associated with less weight gain, colonization of the bile duct with aerobic bacteria Escherichia coli dominating (in 75% of the animals), a shortened hilum-intestine transit time but reduced liver clearance in dynamic biligraphy, and fibrous periportal changes in liver histology (in 50% of the animals). We conclude that during 1 y follow-up HJ with no anastomotic stricture formation is associated with improved extrahepatic bile drainage, but with ascending contamination of bile ducts with bacteria, which might be involved with the fibrous periportal changes in liver histology in diminished excretion of Tc-HIDA from the hepatocytes into the bile. The clinical significance of these changes, and the reduced weight gain observed is a topic of further investigations. © 2007 Elsevier Inc. All rights reserved.

Key Words: hepaticojejunostomy; cholecystectomy; bile flow; bile composition; cholecystography.

INTRODUCTION

Hepaticojejunostomy (HJ) is a common operation, not only to by-pass extrahepatic biliary obstructions, but also to establish biliary-enteric continuity after resections for benign and malignant diseases. In most of the patients, biliary reconstruction is considered to afford satisfactory long-term outcome with no symptoms or rise of the serum liver values. However, 7 to 38% of patients have been reported to develop anastomotic strictures, leading to the need for subsequent treatment with percutaneous transhepatic dilation, endoscopic dilation, or operative revision [1–4]. In the overwhelming majority of patients, HJ does not cause detectable major complications. It is known that the destruction of the sphincter of Oddi by endoscopic sphincterotomy results in ascending contamination of the initially sterile bile duct in rabbits [5] and in man [6], as well as in enhanced common bile duct drainage [7], but hepatic changes have not been reported. Despite the fact that HJ is a common operation, knowledge about the changes in hepatobiliary physiology after the operation is surprisingly limited.

The aim of the present study was to investigate in a swine model the changes in overall health and weight, biliary dynamics, bile composition and hepatic histology induced by Roux-Y HJ.
MATERIALS AND METHODS

Twenty-four Yorkshire swine [weight median 57 (range 47 to 76) kg] underwent cholecystectomy. In addition, half of the swine either underwent Roux-en-Y HJ (Group I; HJ; n = 12) or were left without any biliodigestive anastomosis (Group II; no HJ; n = 12). The animals were followed up for 6 or 12 mo by repeated blood, serum, and bile analysis, 99mTechnetium (Tc) diethyliomindoacetic acid (HIDA) dynamic biligraphy, and histological analysis of the liver and hepatic duct samples. The animals were fed with standard pig chow and were allowed free access to water and free movement in their cages. For all of the experiments and operations, anesthesia was induced after 2-day fast by 5% halothane (Naracotan, Léčiva, Czech Republic) inhalation after ketamine (Ketalar; Pfizer, Hameln Pharmaceuticals GmbH, Hamlin, Germany) 10 mg/10 kg i.m. premedication, and maintained by 2% halothane inhalation vaporized with 100% oxygen after intubation with a cuffed endotracheal tube. In the induction of the anesthesia before the operations, the animals received amoxicillin (Amoxin; Merckle GmbH, Blaubeuren, Germany) 5 mg/10 kg i.v. All of the operations were performed by one surgeon (JL).

In all 24 animals, an upper midline laparotomy was performed, liver sampled, and gallbladder bile aspirated, and kept anaerobic on ice until analysis. The cystic duct was closed by clamping, the common bile duct cannulated with thin (24 gauge) polyethylene tubing and 4 mL of bile duct (hepatic) bile collected. Cholecystectomy was performed, ligating cystic duct and artery with 3-0 polyactic acid sutures (Vicryl; Ethicon, Edingburg, United Kingdom). In Group I (HJ), bile duct was cut proximal to cystic duct and the distal end ligated. Jejunum was transected 15 cm distal to ligament Treitz, and an end-to-side HJ performed with interrupted 5-0 polytrimethylene carbonate (Maxon; Syneture, Norwalk, CT) sutures in one layer. The end-to-side HJ performed with interrupted 5-0 polytrimethylene carbonate (Maxon) interrupted and continuous sutures. In Group II (no HJ), the diameter of the bile duct anastomosis was measured by probing, whereas the distal end of the transected jejunum was closed. An end-to-side enteropancreatectomy in two layers with 4-0 polytrimethylene carbonate (Maxon) interrupted and continuous sutures. In Group II (no HJ), the diameter of the bile duct was estimated by external probes. In both Groups I and II, the abdominal cavity was washed with saline, and the abdomen was closed in two layers. Prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication, and the abdomen was closed in two layers. Prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication, and the abdomen was closed. In Group II (no HJ), the animals were given gentamicin (Amoxin; Merckle GmbH, Blaubeuren, Germany) 5 mg/10 kg i.m. for postoperative antibiotics. In Group I (HJ), ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication, and the abdomen was closed in two layers. Prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication. In both Groups I and II, prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication.

For histology, 4 mL of bile duct (hepatic) bile collected. Cholecystectomy was performed, ligating cystic duct and artery with 3-0 polyactic acid sutures (Vicryl; Ethicon, Edingburg, United Kingdom). In Group I (HJ), bile duct was cut proximal to cystic duct and the distal end ligated. Jejunum was transected 15 cm distal to ligament Treitz, and an end-to-side HJ performed with interrupted 5-0 polytrimethylene carbonate (Maxon; Syneture, Norwalk, CT) sutures in one layer. The diameter of the bile duct anastomosis was measured by probing, whereas the distal end of the transected jejunum was closed. An end-to-side enteropancreatectomy in two layers with 4-0 polytrimethylene carbonate (Maxon) interrupted and continuous sutures. In Group II (no HJ), the diameter of the bile duct was estimated by external probes. In both Groups I and II, the abdominal cavity was washed with saline, and the abdomen was closed in two layers. Prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication, and the abdomen was closed. In Group II (no HJ), the animals were given gentamicin (Amoxin; Merckle GmbH, Blaubeuren, Germany) 5 mg/10 kg i.m. for postoperative antibiotics. In Group I (HJ), ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication, and the abdomen was closed. In both Groups I and II, prior to extubation, ketorolac tromethamine (Toradol; Roche, Basel, Switzerland) 6 mg/10 kg i.m. was given for postoperative pain medication.

In dynamic biligraphy, 99mTc HIDA (volume 1.5 mL, radioactivity 3 mCi) was injected into the cannulated ear vein, and the study performed by obtaining serial analog images for 90 min at 1-min intervals with a γ-camera (Starcam; GE Medical Systems, Huntley, IL). The organs or parts of the organs (liver, liver hilum, and duodenum) were determined within the region of interest (ROI). The registered counts per mCi per ROI were corrected by the Tc half-life and background radiation. Hepatic maximal uptake, hepatic clearance at 15, 90, 45, and 60 min, and the hilum-intestine transit time were determined.

Blood samples aspirated from the femoral vein were analyzed for full blood count and partly centrifuged to obtain serum. Serum samples were analyzed for sodium (S-Na; method: ion selective electrode), potassium (S-K; method: ion selective electrode), creatinine (S-Crea; method: Jaffe reaction), glucose (S-Gluc; method: enzymatic determination), and amylase (S-Amyl; method: kinetic, substrate ED-PNP-maltoheptoside); of the liver function tests, total bilirubin (S-Bil; method: diatro reaction), direct bilirubin (S-Bil-Dir; method: diatro reaction), bile acids (method: enzymatic, colorimetric), alanine aminotransferase (S-ALT; method: kinetic, according to the European Committee for Clinical Laboratory Standards (ECCLS) reference), alkaline phosphatase (ALP; method: kinetic, substrate p-nitro phenyl phosphate in AMP), glutamyltransferase (S-GT; method: kinetic, according to ECCLS reference), and lactate dehydrogenase (S-LDH; method: kinetic, according to Nordic reference) were studied. Total cholesterol (S-T-Chol; method: enzymatic), HDL-cholesterol (S-HDL-C; method: direct enzymatic), LDL-cholesterol (S-IDL-C; method: Friedewald formula), Triglycerides (S-TG; method: enzymatic), total protein (S-Prot; method: photometric), and albumin (S-Allb; method: immunoturbidimetric) were also determined.

A aliquots of bile from the gallbladder and from the hepatic bile duct were frozen for subsequent analysis of bile acids and phospholipids (method: end point enzymatic assay kit; Wako Corp, Osaka, Japan). Determination of the cholesterol and bilirubin concentrations, pH (method: test strips by QA Supplies; Norfolk, VA) and the culture for aerobic and anaerobic bacteria was done immediately following the retrieval of bile. Analysis of histology was performed blinded for the group from the formalin-fixed, paraffin-embedded liver (stained with hematoxylin and eosin, Masson-Goldner’s trichrome and Gomori’s reticulin) and hepatic duct (stained with hematoxylin and eosin) specimens by a specialized pathologist. Semiquantitative analysis of liver histology included grading of (1) portal perportal and/or bridging necrosis, (2) intralobular degeneration and focal necrosis, (3) portal inflammation, and (4) fibrosis according to the histological activity index (HAI; the Knodell score) [8], and (5) centrilobular and perportal cholestasis according to Desmet [9]. In bile duct histology, atrophy, mucosal inflammation, submucosal vascularization, submucosal fibrosis and scar formation were all analyzed semiquantitatively on a scale none, mild, and marked.

The data are shown as mean and SEM or as median and range, as indicated. Student’s t test, χ2-test, Mann-Whitney t-test, and General linear model variance analysis were used to calculate the statistical significance of the differences. Differences of P ≤ 0.05 were considered statistically significant.

The study was conducted in accordance with the Helsinki Declaration for Scientific Experimentation on Animals. This study was approved by the Institutional Animal Care and Use Committee of the Singapore General Hospital and all animal experiments were carried out at the premises of the Department of Experimental Surgery, Singapore General Hospital.

RESULTS

Preoperatively, the two groups were comparable in terms of weight, bile duct diameter, dynamic biligraphy determinations (liver maximum, hilum-intestine time, liver clearance), and blood, serum, bile duct bile, and gallbladder bile concentrations. All of the animals remained healthy and gained weight during the follow-up period. There was no difference in the weight of animals between the two groups at 3 mo [60 (48 to 64) versus 64 (58 to 72) kg, respectively], but the weight of the Group I (HJ) animals was lower compared with the Group II (no HJ) animals at 6 mo [72 (58 to 77) kg versus 90 (86 to 100) kg; P = 0.01] and at 12 mo [90 (87 to 120) kg versus 145 (128 to 150) kg; P = 0.003], respectively. Blood and serum determinations at 3, 6, and 12 mo did not differ from the preoperative concentrations in Groups I and II or between the two groups.
Preoperatively, the gallbladder bile concentrations of cholesterol, phospholipids, bile acids, and bilirubin were significantly higher and the pH lower compared with the hepatic duct bile concentrations. At 6 and 12 mo, the hepatic duct bile concentrations of cholesterol, phospholipids, bile acids, and bilirubin were significantly diminished and the pH had a tendency to increase compared with the preoperative hepatic duct concentrations (Table 1). In the gallbladder or hepatic duct bile there was no bacterial growth preoperatively either in Group I or in Group II. In the follow-up, there was also no bacterial growth in the hepatic duct bile in Group II (no HJ). Nine of the Group I (HJ) animals had postoperatively aerobic bacterial growth (Escherichia coli) in the hepatic duct bile. No anaerobic bacteria were detected.

In dynamic biligraphy, liver maximum did not differ from the preoperative value in Group I (HJ) or in Group II (no HJ) at 3, 6, or 12 mo postoperatively (Fig. 1). Hilum-intestine time was significantly shorter in Group I animals at 3, 6, and 12 mo compared with the preoperative value and significantly longer in Group II animals at 3, 6, and 12 mo compared with the preoperative value (Fig. 1). In Group II, the liver clearance at 15, 30, 45, and 60 min after the $^{99m}$Tc injection did not differ significantly from the preoperative liver clearance. In Group I, the liver clearance at 15, 30, 45, and 60 min after the $^{99m}$Tc injection was reduced at 3 mo by 16% and at 6 and 12 mo by 23% compared with the preoperative values or to the Group II postoperative values (Fig. 2). The inner diameter of the HJ-anastomosis in Group I animals did not differ at 6 mo [7.3 (6 to 8) mm] or at 12 mo [8 (8 to 9) mm] from the preoperative hepatic duct inner diameter [7.2 (6 to 7) mm]. In Group II (no HJ), the bile duct inner diameter was significantly increased both at 6 mo [$^{99m}$Tc injection was reduced at 3 mo by 16% and at 6 and 12 mo by 23% compared with the preoperative values or to the Group II postoperative values (Fig. 1). The inner diameter of the HJ-anastomosis in Group I animals did not differ at 6 mo [7.3 (6 to 8) mm] or at 12 mo [8 (8 to 9) mm] from the preoperative hepatic duct inner diameter [7.2 (6 to 7) mm]. In Group II (no HJ), the bile duct inner diameter was significantly increased both at 6 mo [9 (8 to 10) mm; $P = 0.038] and at 12 mo [9 (7 to 11) mm; $P = 0.04] from the preoperative bile duct inner diameter [6.7 (5 to 8) mm].

In liver histology, all of the parameters were graded as normal (total score per animal 5) in both Groups I and II preoperatively (total scores per group 60 and 60, Group II (no HJ))

<table>
<thead>
<tr>
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<th>Preoperatively (n = 12)</th>
<th>At 6 mo (n = 6)</th>
<th>At 12 mo (n = 6)</th>
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<td></td>
<td>Median</td>
<td>Range</td>
<td>Median</td>
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<tr>
<td>GB Chol (mmol/L)</td>
<td>4.0*</td>
<td>2.4–4.8</td>
<td>1.1*</td>
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<tr>
<td>GB Phospholipids (mM)</td>
<td>22.5*</td>
<td>19–31</td>
<td>6*</td>
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<tr>
<td>GB Bile acids</td>
<td>77000*</td>
<td>39800–132000</td>
<td>31850*</td>
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<td>GB Bil Tot (umol/L)</td>
<td>525*</td>
<td>36–72</td>
<td>40*</td>
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<td>GB pH</td>
<td>7.0*</td>
<td>6.5–7.5</td>
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$^*P < 0.05$; compared with the preoperative bile duct concentrations in the same group.

### TABLE 1

Gallbladder (GB) and Bile Duct (BD) Bile Concentrations in Group I (Cholecystectomy and Hepaticojejunostomy; HJ) and Group II (Cholecystectomy, no Biliodigestive Anastomosis; no HJ) Preoperatively and at 6 and 12 Months Postoperatively (Median and Range)
respectively), and in all of the Group II (no HJ) animals postoperatively (total scores 30 and 30 per follow-up groups at 6 and 12 mo, respectively). In Group I (HJ), 3/6 animals in the 6-mo follow-up group and 3/6 animals in the 12-mo follow-up group (total 6/12; 50%) had abnormal grading of at least one of the parameters. All six animals had the level of fibrosis graded as 2 (“fibrous portal expansion”) compared with none in Group II (no HJ; \( P \leq 0.006 \)) and, in addition, one of these three animals in both follow-up groups had perportal and/or bridging necrosis graded as 2 (“mild piecemeal necrosis”), plus portal inflammation graded as 2 (“mild”). Thus, the semi-quantitative grading scores for these three animals were 6, 6, and 8 per animal in both follow-up groups, and the total scores per follow-up groups 6 and 12 mo 35 and 35, respectively, compared with the total score 30 per follow-up group in the Group II (no HJ) animals (\( P = 0.006 \)). Intrahepatic degeneration and focal necrosis or cholestasis were not seen in any of the samples. Five out the six Group I (HJ) animals with fibrous portal expansion were those with the most reduced liver clearance at 15, 30, 45, and 60 min after the \(^{99m}\text{Tc} \) injection. In addition, all six with fibrous portal expansion had postoperative aerobic bacterial growth in the hepatic duct bile. No cholangitis was detected during the follow-up in either study group. The hepatic duct histological analysis did not differ between the groups. At 6 and 12 mo postoperatively, all of the parameters studied were considered normal in all of the Group II (no HJ) animals and in 11/12 of the Group I (HJ) animals. One Group I animal in the 6-mo follow-up group had a mild inflammation reaction of the mucosa and mild submucosal vascularization (total score 2).

**DISCUSSION**

In this study, biliary dynamics and the composition of bile and histology of liver and hepatic duct were investigated in a swine model both before and after a successful Roux-en-Y HJ. To our knowledge, this has not been studied before, although such reconstruction is widely used for various purposes. It was found that even though the HJ-anastomosis is fully open and the

![FIG. 1](image1.png)  
**FIG. 1.** Liver maximum and hilum-intestine transit time studied with dynamic biligraphy in Group I (cholecystectomy and hepaticojejunostomy; HJ; open bars) and Group II (cholecystectomy, no biliodigestive anastomosis; no HJ; closed bars) pigs preoperatively and at 3, 6, and 12 mo postoperatively (median and range). *\( P \leq 0.05 \); compared with the preoperative value of the group as well as to the other group at the same time point.

![FIG. 2](image2.png)  
**FIG. 2.** Liver clearance at 15, 30, 45, and 60 min after the \(^{99m}\text{Tc} \) i.v. injection in dynamic biligraphy in Group I (cholecystectomy and hepaticojejunostomy; HJ; black) and Group II (cholecystectomy, no biliodigestive anastomosis; no HJ; gray) pigs preoperatively and at 3, 6, and 12 mo postoperatively (median and range). *\( P \leq 0.05 \); compared with the preoperative value of the group as well as to the other group at the same time point.
hilum-intestine time is even shortened, the liver clearance, as determined with $^{99m}$Tc HIDA dynamic biligraphy, is reduced compared with the same animals preoperatively or to the animals that underwent cholecystectomy alone. This was accompanied with changes in bile duct bile composition, bacterial contamination, and fibrosis in the liver histology. In addition, HJ was associated with lower weight gain compared with cholecystectomy alone.

In humans, several studies have been performed on the complications of HJ, but little is known in the long-term of the detailed hepatobiliary function in asymptomatic patients. In humans, hepatobiliary disease is often related to obstruction of bile flow due to chronic biliary anastomotic stricture formation. Overall 7 to 38% of patients have been reported to develop anastomotic strictures after HJ in median 54 to 80 mo follow-up, resulting in the need for subsequent treatment with percutaneous, transhepatic, or endoscopic dilation or operative revision [1–4]. However, clinical studies on the long-term effects of HJ-anastomosis are rare, especially when it comes to an anastomosis without a stricture. In humans, there is no established clinical correlation between Roux-en-Y hepaticojejunostomy and subsequent liver disease. According to the present study, where no anastomotic strictures were present, some changes in hepatobiliary physiology may also be unrelated to stricture formation.

Because of the similarities of its hepatobiliary system to that of a man, the present study, intended for the study of changes after HJ, was carried out on swine, an animal model widely used in the preclinical hepatobiliary studies. In the swine, the sphincter of Oddi is of Type 2 [10], which is similar in many respects to a human sphincter of Oddi and the diameter of the bile duct in a 60-kg animal resembles human bile duct size. In all of the HJ-operated animals, the bile duct-intestinal anastomosis was found fully open when studied at 6 and 12 mo postoperatively, as judged by liver chemistry, measurement of the anastomosis by probing, and by dynamic biligraphy with Tc-HIDA.

During follow-up, the weight gain in Group II (no HJ) animals was similar to control Yorkshire swine kept under similar laboratory conditions and on similar diet. The HJ-operated animals gained less weight compared with the cholecystectomized animals. This is not because of possible changes in the bile composition, since such could not be detected between the groups. We did not measure caloric intake or quantify fecal fat. However, all of the animals were fed the same amount of standard pig chow and were allowed free access to water and free movement in their pens and, thus, there is no evidence that the nutritional intake was different between the groups. Blood and serum determinations (e.g., liver and cholesterol values, proteins, and albumin) at 3, 6, and 12 mo did not differ from the preoperative measurements in Groups I and II or between the two groups. Thus there was no evidence of malabsorption either.

It is known that biliopancreatic diversion procedure, currently perhaps one of the most popular surgical operations for morbid obesity, is an effective approach to weight loss [11, 12]. According to the present results, HJ operation might also be associated with reduced weight gain. The mechanism of this remains unknown. Possible explanations for the phenomenon might include the following: (1) Enteric anastomosis was not performed in the cholecystectomy (no HJ) group. Originally, the control operation was designed to represent a clinically relevant situation. (2) It is possible that some animals in the HJ group might have had chronic cholangitis, since three quarters of the HJ operated animals developed colonization of the bile duct with aerobic bacteria Escherichia coli dominating. However, there were no signs for acute cholangitis during the follow-up. It is not known whether the possible chronic cholangitis could affect the weight gain in these animals. (3) Theoretically, blind-loop syndrome might have been present is some of the animals, even though there were no (other) signs referring to that. Since studies on the long-term effects of HJ in humans are rare, no reduction in the weight gain in relation to HJ operation has been reported in patients.

Cholecystectomy alone, without HJ, induced an increase in the bile duct diameter. This has also been reported in humans [13] and explained that the bile duct takes over the storage functions after gallbladder removal. It is understandable that biliary diversion, or the exclusion of the sphincter of Oddi, prohibited this phenomenon.

Dynamic biligraphy is a highly sensitive method in identifying partial bile duct obstruction [14], also after stenting or bypass surgery [15]. The hilum time-activity curve and the hilum-intestine time are the most useful tools to study extrahepatic bile duct drainage [14, 16, 17]. The present results indicate that HJ was associated with improved rather than impaired drainage of the extrahepatic bile duct. This is understandable because of the exclusion of the resistor type sphincter of Oddi. However, the slowed excretion of $^{99m}$Tc-HIDA suggested deteriorated liver clearance at the level of the hepatocytes. This could be explained by several possible mechanisms: altered canalicular membrane bile secretion, alterations in the enterohepatic recycling of bile salts, altered FXR-mediated bile salt handling in hepatocytes, and/or hepatocyte loss due to fibrosis. The mechanisms by which chronic colonization of the biliary system by enteric bacteria lead to the scintigraphic findings are likely to be complex.

Three quarters of the HJ operated animals developed colonization of the bile duct with aerobic bacteria Escherichia coli dominating. It has also previously
been shown that the destruction of the sphincter of Oddi by endoscopic sphincterotomy results in ascending contamination of the initially sterile bile duct in rabbits [5] and in man [6]. If, then, biliary obstruction develops, this bactibilia may be an important factor in the pathogenesis of cholangitis, gallstone formation, gallstone pancreatitis [18] and, perhaps, in cholangiocarcinogenesis [19]. Even though in the present study bile flow from bile duct into the intestine seemed to remain undisturbed, disruption of the sphincter of Oddi, allowing enteric bacterial colonization of the hepatic biliary system, may play an important role in the findings made in the study.

Half of the HJ operated animals had an abnormal grading of at least one of the studied parameters in liver histology: fibrous portal expansion alone was seen in four animals, and fibrous portal expansion combined with mild piecemeal necrosis and mild portal inflammation was detected in two animals. These changes were observed in none of the animals without biliary diversion. It might be suggested that these changes were induced by the ascending contamination of the bile ducts with bacteria. In fact, this was supported by the association between bile duct colonization and the fibrous periportal changes in histology. Furthermore, these changes may also explain why liver clearance was decreased, i.e., clearance of Tc-HIDA from the hepatocytes into the bile. This in turn is supported by the fact that the liver clearance was slowest among the six swine with fibrous changes compared with the six swine without such changes. It is not known, however, whether the reduction in the liver clearance detected in this study as well as the liver histological changes would proceed or normalize during longer follow-up time. If the decreased liver clearance proceeded in the course of years, it might also have potential clinical implications on the liver functions. For this, studies with a longer follow-up time are needed.

In conclusion, during 1-y follow-up HJ with no anastomotic stricture formation is associated with improved extrahepatic bile drainage, but with ascending contamination of bile ducts with bacteria, fibrous periportal changes in liver histology, and slowed excretion of Tc-HIDA from the hepatocytes into the bile. The clinical significance of these changes, and the reduced weight gain observed, is a topic of further investigation.

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