ORIGINAL ARTICLE

Biliary Complications After Hepatic Resection

Risk Factors, Management, and Outcome

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Objective: To identify the risk factors for the development of biliary complications after hepatic resection and to evaluate management in relation to the outcomes of these patients.

Design: Biliary complications are a common cause of major morbidity after hepatic resection. A survey was made of all patients undergoing hepatic resection at 1 institution. Perioperative risk factors related to the development of biliary complications were identified using multivariate analysis. Management and outcome were analyzed also.

Setting: A tertiary referral center.

Patients: From January 1, 1989, to October 31, 1995, 347 consecutive patients underwent 229 major and 118 minor hepatic resections.

Main Outcome Measure: Development of postoperative biliary complications.

Results: Biliary complications developed in 28 (8.1%) of 347 patients; these complications carried high risks for liver failure (35.7%) and operative mortality (39.3%). Stepwise logistic regression analysis identified increasing age, higher preoperative white blood cell count, left-sided hepatectomy, and prolonged operation time as the independent predictors of development of biliary complications. Conservative treatment or nonoperative measures alone, such as percutaneous drainage or endoscopic therapy, were effective in treating the complication in 13 of 19 patients, but those who required reoperation had a high mortality rate (7 [77.8%] of 9 patients). Patients with demonstrable leakage from the common bile duct or its bifurcation tended to have poor outcomes.

Conclusions: Biliary complications are a common and serious cause of morbidity after hepatic resection. Preresection cholangiography for finding biliary tract anomaly is recommended before left-sided hepatectomy. Although nonoperative measures are the preferred approach for selected patients with biliary complications, those with demonstrable leakage from the common bile duct or its bifurcation have a grave prognosis and may benefit from early surgical intervention.

Arch Surg. 1998;133:156-161

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BECAUSE OF recent advances in liver surgery, hepatic resections are more frequently performed, with a reduction in operative mortality rates.[1-6] Despite a significant decrease in overall operative morbidity, the rate of biliary complications has not changed.[6] Biliary complications remain a common cause of major morbidity after hepatic resection, with an incidence of 4.8% to 7.6% reported in recent large series.[2-7] The presence of bile in the dead space after liver resection predisposes to the development of sepsis, which is a well-known cause of liver failure and death.[8,9] The purpose of our retrospective study was to identify the risk factors for the development of biliary complications after hepatic resection and to evaluate management in relation to the outcome of these patients.

RESULTS

INCIDENCE

There were no intraoperative deaths or deaths within 24 hours of the operation. Biliary complications occurred in 28 (8.1%) of 347 patients. Although the operative mortality rate was significantly reduced from 12.3% in the early period to 4.8% in the later period ($P=.01$), there was no significant change in the biliary complication rate (9.4% vs 6.5%; $P=.31$). The

PATIENTS AND METHODS

The medical records of 347 patients who underwent hepatic resection at the Department of Surgery, University of Hong Kong, Queen Mary Hospital, from January 1, 1989, to October 31, 1995, were studied retrospectively. There were 251 male and 96 female patients, with a mean age of 53 years (range, 2-86 years). The indications for surgery are seen in the following tabulation:

Diagnosis	No. of Patients
Malignant neoplasia	285
Hepatocellular carcinoma	211
Colorectal liver metastases	34
Peripheral cholangiocarcinoma	14
Hilar cholangiocarcinoma	10
Other malignant tumors	16
Benign lesions	62
Intrahepatic lithiasis	46
Other benign liver lesions	16

Two hundred twenty-nine patients (66.0%) underwent major hepatic resection (defined as resection of ≥3 liver segments, as described by Couinaud[10]).

SURGICAL TECHNIQUE

Our technique of hepatic resection has been described previously.[4] Laparotomy was performed through a bilateral subcostal incision with a midline extension in 324 patients; a bilateral subcostal incision with an additional thoracic extension in 13 patients; a midline incision in 6 patients; and a thoracoabdominal incision in 4 patients. Thorough intraoperative ultrasonography was performed to determine the extent of disease and the line of parenchymal transection so that we could obtain an optimal tumor-free margin and avoid major vessels at the transection plane. Preoperative cholangiography usually was not performed. For hemihepatectomy or extended operations, hilar dissection was performed to divide the ipsilateral branch of the hepatic artery and portal vein. The hepatic duct, however, was not dissected at this stage. Instead, it was divided inside the liver, as it was exposed during parenchymal transection. The stump of the hepatic duct was ligated or oversewn with fine absorbable sutures. From 1989 to 1992 (the early period), the crushing clamp method was used in most patients to transect the liver parenchyma, and an intermittent Pringle maneuver was applied. From 1993 to 1995 (the later period), parenchymal transection was performed primarily using an ultrasonic dissector, largely without any vascular inflow occlusion.

Following hepatic resection, various modifications in technique were adopted to detect and prevent biliary complications. Intraoperative cholangiography was performed for selected patients when the integrity of the bile duct was in doubt. T-tube drainage of the biliary tree was used after concomitant bilioenteric anastomosis or when deemed necessary by the surgeon. Whenever possible, the greater omentum was used to cover the cut surface of the liver. In the later period, injection of a diluted methylene blue solution via the cystic duct was performed to exclude occult bile leakage, and fibrin glue was applied to the raw surface of the liver to promote hemostasis and to prevent bile leakage. Abdominal drains were routinely employed throughout the study. Drains were removed when the drainage was serous and not bile stained, usually around the fifth postoperative day. Systemic antibiotics (third-generation cephalosporins) were administered on induction of anesthesia and for 2 doses after the operation, unless clinically contraindicated.

DEFINITIONS

The diagnosis of biliary complication was based on the postoperative findings of 1 or more of the following: (1) drainage of bile from the abdominal wound or drain; (2) intraabdominal collection of bile confirmed at the time of reoperation or percutaneous drainage; and (3) cholangiographic evidence of biliary leakage or stricture. Patients in whom bile leakage was detected and corrected during the hepatic resection and in whom postoperative biliary complications did not develop were excluded. For the purpose of our study, major bile leakage was defined as demonstrable leakage from the common bile duct or its bifurcation. Minor leakage included leakage from the raw surface of the liver or a site that could not be identified using cholangiography or reexploration. Cholangiography included intraoperative, T-tube, and percutaneous transhepatic cholangiography and endoscopic retrograde cholangiopancreatography. Operative mortality was defined as death within 30 days of hepatic resection or within the same hospital admission for surgery. All patients had a minimum follow-up of 3 months or until death.

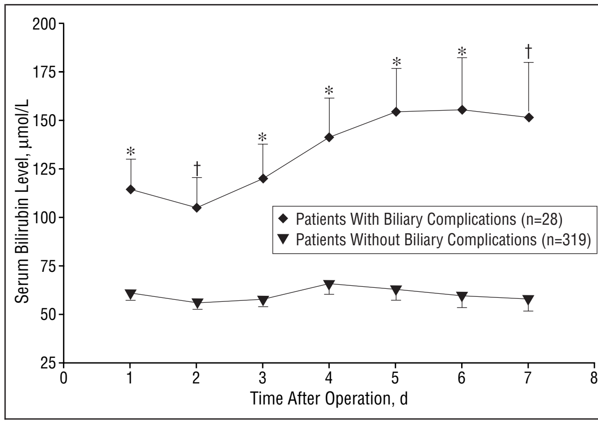
STATISTICAL ANALYSIS

Patients with and without biliary complications were compared with reference to 31 preoperative and operative variables. Preoperative parameters included sex; age; presence of diabetes mellitus; time of operation (early or later period); diagnosis of malignant liver tumor; diagnosis other than hepatocellular carcinoma; hemoglobin level; white blood cell and platelet counts; serum levels of urea, total bilirubin, and albumin; prothrombin time; and Child grade.[11] Operative variables included extent of hepatic resection (major or minor); performance of left-sided hepatectomy (hemihepatectomy, extended hepatectomy, or trisegmentectomy); concomitant caudate resection; use of the Pringle maneuver, an ultrasonic dissector, various techniques in detecting and preventing bile leakage (including methylene blue test), greater omentum to cover raw surface of liver, and fibrin glue, postoperative cholangiogram, and T-tube drainage; concomitant bowel resection or bilioenteric anastomosis; absence of cirrhosis in the liver remnant; intraoperative hypotension of greater than 80 mm Hg; operation time; operative blood loss; and transfusion requirement. Continuous variables were expressed as mean±SEM and compared using the Student *t* test. Categorical variables were compared using the χ^2 test or Fisher exact test where appropriate. Variables significant at a level of $P<.10$ on univariate analysis were subjected to stepwise logistic regression analysis to identify the independent predictors of biliary complications. The perioperative variables of survivors and nonsurvivors of biliary complications were also compared using Mann-Whitney *U* test, χ^2 test, or Fisher exact test. All statistical analysis was performed using SPSSPC+ (SPSS Inc, Chicago, Ill), and $P<.05$ was taken as statistically significant.

Table 1. Types of Hepatic Resection and Incidence of Biliary Complications

Operation	No. of Patients (No. of Concomitant Caudate Resections)	Biliary Complication, No. of Patients (%)
Major*		
Right hemihepatectomy	118 (9)	11 (9.3)
Right extended hepatectomy	32 (2)	1 (3.1)
Right trisegmentectomy	30 (7)	2 (6.7)
Left hemihepatectomy	32 (4)	6 (18.8)
Left extended hepatectomy	14 (2)	3 (21.4)
Left trisegmentectomy	3 (0)	2 (66.7)
Minor†		
Left lateral segmentectomy	61 (0)	2 (3)
Segmentectomy	25 (0)	0 (0)
Subsegmentectomy	32 (0)	1 (3.1)

*Includes 229 patients.
†Includes 118 patients.



Mean (SEM) postoperative serum bilirubin levels in patients with and without biliary complications after hepatic resection. Asterisk indicates P<.005; dagger, P<.01.

Table 2. Site of Biliary Leakage According to Different Types of Hepatic Resection

	Type of Resection, No. of Patients		
Site	Right-sided*	Left-sided*	Minor
Hepatic duct stump	4	2	0
Bilioenteric anastomosis	1	3	0
Common hepatic duct	1	2	0
Raw surface of liver	1	1	0
T-tube insertion	1	0	0
Unknown	6	3	3
Total	**14**	**11**	**3**

*Includes hemihepatectomy, extended hepatectomy, and trisegmentectomy.

biliary complication rate of left-sided hepatectomy (22.5%) was significantly higher than that of minor (2.5%; *P*<.001) or right-sided hepatectomy (7.8%; *P*=.004) (**Table 1**). The complication rate for left-sided hepatectomy increased with the extent of resection, from 18.8% for hemihepatectomy to 66.7% for trisegmentectomy. When compared with patients without biliary complications, those with biliary complications were at increased risk for operative mortality (39.3% vs 6.0%; *P*<.001), liver failure (35.7% vs 6.9%; *P*<.001), and a prolonged hospital stay (59 vs 19 days; *P*<.001).

CLINICAL PRESENTATION

Clinical presentation of biliary complications included biliocutaneous fistula in 17 patients (drainage of bile from the main wound in 1 patient and from drains placed at the end of operation in 16 patients), intra-abdominal sepsis in 6 patients, features of peritonitis in 4 patients, and hemoperitoneum with shock in 1 patient. Among various postoperative hematologic and biochemical tests, including white blood cell and platelet counts and total bilirubin, alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase serum levels, only the total bilirubin level was persistently higher in patients with biliary complications (**Figure**).

The site of biliary leakage with or without stricture, identified using cholangiography or reoperation, included the hepatic duct stump of the resected lobe in 6 patients, bilioenteric anastomosis in 4 patients, common hepatic duct in 3 patients, raw surface of liver in 2 patients, and T-tube insertion site in 1 patient. In the remaining 12 patients, the leakage site could not be identified (**Table 2**). Aerobic and anaerobic culture of the drained bile revealed microbial isolates in 23 of 28 patients, including *Staphylococcus aureus* in 4 patients, *Escherichia coli* in 3 patients, *Candida* species in 3 patients, *Pseudomonas* species in 2 patients, mixed growth in 7 patients, and *Streptococcus faecalis, Streptococcus mulleri,* and *Morganella* and *Bacillus* species in 1 patient each.

RISK FACTORS

Six preoperative and 8 operative factors were associated with the development of biliary complications using univariate analysis (**Table 3**). Among these 14 variables, stepwise logistic regression analysis identified age (coefficient, 0.038; *P*=.04), preoperative white blood cell count (coefficient, 0.164; *P*=.006), left-sided hepatectomy (coefficient, 1.049; *P*=.04), and operation time (coefficient, 0.004; *P*=.003) as the only independent risk factors for the development of biliary complications.

MANAGEMENT AND OUTCOME

Depending on the presentation and the clinical condition of these 28 patients, the initial treatment of biliary complications consisted of reoperation in 9 (7 died), percutaneous drainage of intra-abdominal bile collection in 9 (3 died), endoscopic papillotomy with or without stenting in 4 (1 died), and conservative management in 6 (none died).

Reoperation as the initial treatment was performed at a median of 9 days (range, 1-31 days) after hepatic

Table 3. Factors Associated With Development of Biliary Complications Using Univariate Analysis*

Variables	Patients With Complications (n=28)	Patients Without Complications (n=319)	*P*
Mean±SEM age, y	60±2.5	53±0.8	.009
Nonhepatocellular carcinoma	16	120	.04
Mean±SEM hemoglobin level, g/L	12.3±0.5	13.3±0.1	.02
Mean±SEM white blood cell count, $\times 10^9$/L	9.5±0.8	7.8±0.2	.06
Mean±SEM platelet count, $\times 10^9$/L	263±24	219±6	.03
Child grade B or C	6	22	.02
Major hepatectomy	25	204	.007
Left-sided hepatectomy†	11	38	<.001
Caudate resection	5	19	.03
Use of T-tube drainage	9	45	.03
Concomitant bilioenteric anastomosis	11	31	<.001
Concomitant bowel resection	3	6	.03
Noncirrhotic liver	21	148	.004
Mean±SEM operation time, min	450±38	327±7	.003

**Unless otherwise indicated, data are given as number of patients.*
†Includes hemihepatectomy, extended hepatectomy, and trisegmentectomy.

Table 4. Comparison of Perioperative Variables in Survivors and Nonsurvivors of Biliary Complications

Variables	Survivors (n=17)	Nonsurvivors (n=11)
Sex, No. of M:F	10:7	9:2
Median age, y (range)	57 (35-76)	67 (38-79)
Early period, No. of patients*	8	9
Nonhepatocellular carcinoma, No. of patients	10	6
Preoperative laboratory test results, median (range)		
White blood cell count, $\times 10^9$/L	8.3 (3.7-18.9)	8 (5.6-24.9)
Urea, mmol/L	5.8 (2.5-22.3)	5.8 (3.7-29.3)
Bilirubin, μmol/L	9 (3-105)	15 (5-366)
Albumin, g/L	42 (24-53)	39 (26-46)
Prothrombin time, s > control	0.2 (0-3.4)	0 (0-3.8)
Child grade B or C, No. of patients	4	2
Major hepatectomy, No. of patients	15	10
Left-sided hepatectomy, No. of patients	7	4
Cirrhotic liver, No. of patients	3	1
Median operation time, min (range)	380 (165-855)	465 (210-930)
Median operative blood loss, L (range)	2.4 (0.7-8.0)	1.9 (0.6-6.5)
Positive microbial isolates from bile, No. of patients	14	9
Major bile leakage, No. of patients	6	8†
Median time to first treatment, d (range)	14 (5-31)	10 (1-31)

**Defined in the "Patients and Methods" section of the text.*
†*P*=.05.

resection in 9 patients with features of generalized peritonitis or hemoperitoneum or when nonoperative measures were considered ineffective. Six of these 9 patients had major bile leakage, and 7 of them died after reoperation within the same hospital stay. Two patients with bile leakage from the common hepatic duct after a right- or left-sided trisegmentectomy underwent hepaticojejunostomy within 5 days after initial hepatic resection. One patient survived, and the other died of liver failure. Two other patients underwent laparotomy and drainage of intra-abdominal bile collection. One died of multiple system organ failure, and the other survived. Reoperation in 2 patients was complicated by dense adhesions that rendered dissection and identification of the leakage site difficult. Another 2 patients with leakage from the bilioenteric anastomosis after hepatectomy for hilar cholangiocarcinoma had persistent sepsis after revision of the anastomosis. All 4 patients eventually died of persistent sepsis. The only patient who exhibited hemoperitoneum and shock from ruptured right hepatic artery aneurysm secondary to biliary leakage 1 month after hepatic resection died soon after reoperation.

Percutaneous drainage was the initial procedure of choice in 9 patients when a localized intra-abdominal fluid collection was identified using imaging studies. Two of these died of persistent sepsis despite undergoing laparotomy. Two others underwent additional endoscopic papillotomy to facilitate bile drainage into the duodenum. Biliary leakage failed to resolve, and both underwent reoperation. One patient died, and the other survived. The remaining 5 patients (1 patient requiring temporary percutaneous transhepatic biliary drainage) recovered following percutaneous drainage (once in 2 patients, twice in 2 patients, and 3 times in 1 patient).

Endoscopic therapy (endoscopic papillotomy with or without stenting) was used as the initial treatment in 4 patients with biliocutaneous fistulae to facilitate bile drainage into the duodenum. Three patients recovered, but 1 patient died of persistent sepsis after a laparotomy. The remaining 6 patients with a low-output controlled biliary fistula were treated conservatively and discharged from the hospital. Five of these had resolution within 2 months, but intra-abdominal bleeding from a ruptured hepatic artery aneurysm developed in the other patient 5 months after the initial hepatectomy, and he died of sepsis following transarterial hepatic artery embolization. Thus, among 19 patients treated initially with nonoperative measures, biliary fistulae healed in 13 of 14 patients with nonoperative measures alone. The other 5 patients subsequently underwent reoperation, and only 1 patient survived.

The perioperative variables of survivors and nonsurvivors of biliary complications are compared in **Table 4**. A demonstrable leakage from the common bile duct or its bifurcation was the only factor that was associated with a fatal outcome (*P*=.05).

COMMENT

Biliary complications after hepatic resection are serious and are associated with a liver failure rate and mortality rate of nearly 40%. The presence of bile, blood, and devitalized tissue in the dead space after hepatic resection provides the ideal environment for bacterial growth. The combination of a sudden reduction in the liver volume and development of intraperitoneal sepsis frequently results in liver failure,[9] which has a grave prognosis. Despite a general improvement in perioperative results attributed to various advances in hepatic resection techniques, our report shows that the incidence of biliary complications has not changed. Use of neither the ultrasonic dissector nor the techniques aimed at detecting and preventing biliary complications independently affects the development of biliary complications. The ultrasonic dissector has been adopted by many surgeons in hepatic resection, but its theoretic advantage in reducing the risk of biliary leakage from open bile ducts remains to be proven. A negative result of the methylene blue test or a normal finding of an intraoperative cholangiogram following resection cannot exclude biliary leaks, since damage to the bile duct of a small segregated segment of the liver may continue to cause bile leakage without communication with the main biliary tree.[12] In a randomized study, the use of fibrin glue had no effect on the incidence of bile leakage.[13] T-tube drainage of the common bile duct is used occasionally to decompress the biliary tree in patients at risk for biliary leakage after hepatic resection. Our results supported the view that it did not prevent bile leakage and had, in fact, resulted in bile leakage at the T-tube insertion site in 1 patient.

USING MULTIVARIATE analysis, our study showed that increasing age, higher preoperative white blood cell count, left-sided hepatectomy, and prolonged operation time were 4 independent risk factors for the development of biliary complications. Age was found to be a risk factor for morbidity after hepatic resection by Yamanaka et al,[14] but others found no significant association.[15,16] Most of these postoperative complications, however, are not related to age but to specific infirmities seen mainly in the elderly.[16] The exact cause of the higher incidence of biliary complications in the older patients was not apparent in our study, although diabetes mellitus was not shown to be related. According to a study by Yanaga et al,[9] intraperitoneal septic complications after hepatic resection also were more common in the elderly. Hence, infection and biliary leakage may be closely interrelated. Infection may precipitate biliary leakage by inducing tissue necrosis, whereas bile in the dead space after hepatic resection, in turn, predisposes to infection.

Anatomical problems account for the higher incidence of biliary complications following left-sided hepatectomy. Bile ducts from the caudate lobe and, not infrequently, the right posterior segment duct drain into the left duct[17] and are at risk for damage if the left duct is divided close to the hilum. To delineate possible anatomical variations in the biliary tract, we recommend cholangiography performed before (not after) left-sided hepatic resection, particularly if extended hepatectomy or trisegmentectomy is necessary. In addition, instead of dividing the left hepatic duct at the liver hilum, it should be divided inside the liver, as it is exposed during parenchymal transection.

The causal relationship between prolonged operation time and an increased risk for biliary complications is less clear. Theoretically, surgical error that results in biliary complications can be avoided only by meticulous surgical technique and longer operation time. However, when the same meticulous approach is adopted, the prolongation of operation time and the biliary complications may be the result of a technically difficult and complicated operation.

The results of nonoperative management of biliary leakage after liver transplantation[18] and other biliary tract surgery[19,20] are encouraging, and nonoperative measures have become the preferred approach. A review of 77 cases of endoscopic management of postoperative biliary leakage,[20] mostly following cholecystectomies, suggested that the site of leakage may be related to the success of treatment. Our study supports a similar approach for patients with biliary complications after hepatic resection, and the site of bile leakage has probable prognostic significance. Eight (57.1%) of 14 patients with leakage from the common bile duct or hepatic duct died, compared with 3 (21.4%) of 14 patients with leakage from the raw surface or an unknown site. The amount of leakage from small ducts on the raw surface usually is small and the sites will close spontaneously when the main ducts are patent or when biliary drainage is facilitated by nonoperative measures. On the other hand, leakage from a major duct is a more serious problem that will persist, and these patients are more likely to require surgical intervention. The mortality rate of patients who require reoperation due to biliary complications is considerable (77.8%), because their sepsis is usually more severe, with generalized peritonitis, and they do not have a localized collection or controlled fistula. In addition, dissection in the presence of sepsis after hepatic resection is never easy because of the dense adhesions,[21] particularly if reoperation is decided late in the postoperative period. The tissue trauma and bleeding aggravate the hepatic failure and contribute to the dismal prognosis. Therefore, for patients with demonstrable major bile leakage after hepatic resection, the decision for reexploration should be made as early as possible, preferably before the development of severe sepsis and dense adhesions.

In conclusion, biliary complications after hepatic resection are associated with a high risk for liver failure and operative mortality. A cholangiogram for detection of biliary tract anomaly is recommended before left-sided hepatectomy. When biliary complications occur, the majority of these patients can be treated conservatively or with nonoperative measures such as percutaneous drainage and endoscopic therapy. However, those with demonstrable leakage from the common bile duct or hepatic duct have a grave prognosis, and early surgical intervention should be considered.

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REFERENCES

1. Lai ECS, Fan ST, Lo CM, Chu KM, Liu CL, Wong J. Hepatic resection for hepatocellular carcinoma: an audit of 343 patients. *Ann Surg.* 1995;221:291-298.
2. Bismuth H, Chiche L, Castaing D. Surgical treatment of hepatocellular carcinomas in noncirrhotic liver: experience with 68 liver resections. *World J Surg.* 1995; 19:35-41.
3. Doci R, Gennari L, Bignami P, et al. Morbidity and mortality after hepatic resection of metastases from colorectal cancer. *Br J Surg.* 1995;82:377-381.
4. Fan ST, Lai ECS, Lo CM, Chu KM, Liu CL, Wong J. Hepatectomy with an ultrasonic dissector for hepatocellular carcinoma. *Br J Surg.* 1996;83:117-120.
5. Miyagawa S, Makuuchi M, Kawasaki S, Kakazu T. Criteria for safe hepatic resection. *Am J Surg.* 1995;169:589-594.
6. Tsao JI, Loftus JP, Nagorney DM, Adson MA, Ilstrup DM. Trends in morbidity and mortality of hepatic resection for malignancy: a matched comparative analysis. *Ann Surg.* 1994;220:199-205.
7. Shimada M, Matsumata T, Akazawa K, et al. Estimation of risk of major complications after hepatic resection. *Am J Surg.* 1994;167:399-403.
8. Norton L, Moore G, Eiseman B. Liver failure in the postoperative patient: the role of sepsis and immunologic deficiency. *Surgery.* 1975;78:6-13.
9. Yanaga K, Kanematsu T, Takenaka K, Sugimachi K. Intraperitoneal septic complications after hepatectomy. *Ann Surg.* 1986;203:148-152.
10. Couinaud C. *Le Foie: Etudes Anatomiques et Chirugicales.* New York, NY: Masson Publishing; 1957:9-12.
11. Pugh RNH, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding varices. *Br J Surg.* 1973;60:646-649.
12. Neuhaus P. Complications of liver surgery and their management. In: Lygidakis NJ, Tytgat GNJ, eds. *Hepatobiliary and Pancreatic Malignancies: Diagnosis, Medical and Surgical Management.* New York, NY: Thieme-Stratton Inc; 1989:254-259.
13. Kohno H, Nagasue N, Chang YC, Taniura H, Yamanoi A, Nakamura T. Comparison of topical hemostatic agents in elective hepatic resection: a clinical prospective randomized trial. *World J Surg.* 1992;16:966-970.
14. Yamanaka N, Okamoto E, Kuwata K, Tanaka N. A multiple regression equation for prediction of posthepatectomy liver failure. *Ann Surg.* 1984;200:658-663.
15. Ezaki T, Yukaya H, Ogawa Y. Evaluation of hepatic resection for hepatocellular carcinoma in the elderly. *Br J Surg.* 1987;74:471-473.
16. Stimpson REJ, Pellegrini CA, Way LW. Factors affecting the morbidity of elective liver resection. *Am J Surg.* 1987;153:189-196.
17. Mizumoto R, Suzuki H. Surgical anatomy of the hepatic hilium with special reference to the caudate lobe. *World J Surg.* 1988;12:2-10.
18. Sherman S, Shaked A, Cryer HM, Goldstein LI, Busuttil RW. Endoscopic management of biliary fistulas complicating liver transplantation and other hepatobiliary operations. *Ann Surg.* 1993;218:167-175.
19. Davids PHP, Rauws EAJ, Tytgat GNJ, Huibregtse K. Postoperative bile leakage: endoscopic management. *Gut.* 1992;33:1118-1122.
20. Binmoeller KF, Katon RM, Shneidman R. Endoscopic management of postoperative biliary leaks: review of 77 cases and report of two cases with biloma formation. *Am J Gastroenterol.* 1991;86:227-231.
21. Pace RF, Blenkharn JI, Edwards WJ, Orloff M, Blumgart LH, Benjamin IS. Intraabdominal sepsis after hepatic resection. *Ann Surg.* 1989;209:302-306.

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Association of Tuberculosis Risk With the Degree of Tuberculin Reaction in HIV-Infected Patients

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Background: The risk of developing active tuberculosis associated with a different size of induration to purified protein derivative (PPD) has not been prospectively assessed among individuals infected with human immunodeficiency virus (HIV). The quantification of this risk is important to more appropriately identify candidates for preventive therapy for tuberculosis.
Methods: A prospective, multicenter, cohort study on tuberculosis in HIV-infected patients was conducted in 23 infectious disease units in public hospitals in Italy. Two thousand six hundred ninety-five HIV-infected patients were enrolled in the study. Of these, 1054 patients who were nonanergic at the time of entry were included in the present analysis. The median duration of follow-up was 102 weeks. The main outcome measure was a diagnosis of active tuberculosis confirmed by the isolation of *Mycobacterium tuberculosis* in culture.
Results: Among the 252 patients with PPD reactivity, patients with an induration to PPD of 2 to 4 mm had a median $CD4^+$ lymphocyte count of $0.34 \times 10^9/L$ (interquartile [IQ] range, 0.14×10^9-0.56×10^9), those with a response of 5 to 9 mm had a median count of $0.38 \times 10^9/L$ (IQ range, 0.24×10^9-0.56×10^9), and those with a response of 10 mm or higher had a median count of $0.37 \times 10^9/L$ (IQ range, 0.23×10^9-0.52×10^9) ($P = .38$). Compared with the 802 nonanergic PPD-negative patients, hazard ratios of tuberculosis were 2.1 (95% confidence interval [CI], 0.2-18.3) among the 55 patients with a response to PPD of 2 to 4 mm, 5.7 (95% CI, 1.6-19.8) among the 128 patients with a response to PPD of 5 to 9 mm, and 23.1 (95% CI, 7.8-68.6) among the 69 patients with a response to PPD of 10 mm or higher.
Conclusions: Among nonanergic HIV-infected patients, the degree of response to tuberculin does not appear to reflect the degree of immunosuppression and is strongly correlated with the subsequent incidence of tuberculosis. To identify HIV-infected patients who are at an increased risk of tuberculosis and may benefit from preventive therapy, a response to PPD of 5 mm appears to be an appropriate cutoff point. *Arch Intern Med. 1997;157:797-800*

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