Intra-Abdominal Sepsis After Hepatic Resection

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One hundred and thirty hepatic resections performed over an 8-year period were reviewed for evidence of postoperative intra-abdominal sepsis. Of 126 patients who survived for more than 24 hours after operation, 36 developed culture positive intra-abdominal collections (28.6%). Significant independent variables associated with the development of intra-abdominal sepsis were diagnoses of trauma or cholangiocarcinoma, and the need for reoperation to control hemorrhage during the postoperative period. Before 1984, infected fluid collections were treated predominantly by operative drainage, but this has largely been replaced by percutaneous methods, which have proven effective in most cases. Eighteen (50%) of the infections were caused by a mixed bacterial culture, with *Streptococcus faecalis*, *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Escherichia coli* being the most common isolates. Six patients with clinical signs of sepsis had a sterile fluid collection drained with complete relief of symptoms. This review suggests that intra-abdominal sepsis is a frequent complication after hepatic resection, and can often be managed successfully by nonoperative percutaneous drainage.

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POSTOPERATIVE INTRA-ABDOMINAL sepsis is a well-recognized complication after hepatic resection.[1,2] Although usually performed in the absence of gross bacterial contamination, hepatic resection often results in a large dead space with devitalized tissue at the line of resection. This may reduce the inoculum required for the development of infection;[3] moreover, the presence of blood and bile in the peritoneal cavity may impair the normal host defense mechanisms.[4,5] Classically, postoperative subphrenic or perihepatic abscess has been managed by reoperation,[6] but modern imaging and percutaneous radiologic techniques now offer an alternative nonoperative therapeutic modality.[7,8]

We have reviewed a series of patients who have undergone hepatic resection in the Hepatobiliary Surgery Unit at the Hammersmith Hospital, London, to identify the risk factors associated with the development of posthepatectomy intra-abdominal infection, and to evaluate the changing trends in management.

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Submitted for publication: July 20, 1988.

Patients and Methods

The case records of 127 patients who underwent hepatic resection between 1979 and 1988 were reviewed for evidence of intra-abdominal infection developing during the postoperative period.

The techniques employed for hepatic resection followed well-established guidelines,[9] usually with blunt transection of the hepatic parenchyma following initial hilar dissection and ligation of the appropriate arterial and portal branches. A Pringle maneuver, using a soft vascular clamp placed across the porta hepatis, was frequently used to reduce blood loss. When necessary, biliary reconstruction was performed by means of a 70-cm Roux-en-y jejunal loop, usually with the biliary anastomosis stented by a small silastic catheter to permit cholangiography during the postoperative period. The residual cavity was drained by large-bore silastic drains, which were connected to a closed collecting system. Drains were usually left in place until the drainage fluid was serous and the daily losses were below 100 ml. Prophylactic antibiotics were routinely administered with the induction of anesthesia and were frequently continued for 72 hours after completion of surgery. Before 1981, prophylaxis usually consisted of three antibiotics (tobramycin, cefamandole, metronidazole); since that time, we have used a double antibiotic regime consisting of piperacillin and gentamicin.

Intra-abdominal infection was suspected when the patient had a persistent postoperative pyrexia in the absence

of wound, urinary or pulmonary complications, or developed unexplained clinical deterioration. Most patients were then investigated by ultrasonography or computed tomography (CT) scanning in an attempt to identify a localized fluid collection that might be the source of sepsis. Once identified, the presence of a postoperative perihepatic fluid collection in a patient with clinical symptoms of sepsis was taken as suggesting evidence of an intra-abdominal infection. Confirmation of the presence of intra-abdominal infection was obtained by a positive culture of fluid from the abdominal cavity; this was performed either at the time of reoperation or at the time of initiation of percutaneous drainage. The various methods used to treat the postoperative intra-abdominal infection were noted, as was the need for further operative or nonoperative intervention at a later date.

Statistical significance was evaluated using the chi-square or Student's t-test in a univariate analysis, and significant variables were then analyzed for independence using a stepwise discriminant analysis (BMDP Statistical Software Programs, W.J. Dixon, Ed. Manufacturer, Berkeley, University of California Press, 1987).

Results

From 1979 to 1988, 130 hepatic resections were performed in 127 patients ranging in age from 1 to 75 years (mean of 43.2 years). The 30-day mortality was ten of 108 patients in elective cases (9.3%) and eight of 22 patients (36.3%) where resection was performed after liver trauma. The indications for resection were primary hepatic malignancy in 50 cases (38.5%), metastatic disease in 35 cases (26.9%), benign disease in 23 cases (17.7%), and trauma in 22 cases (16.9%) (Table 1). The resections performed were extended hepatectomy in 35 cases (26.9%), hepatectomy in 58 cases (44.6%), and left lateral or segmental hepatic resections in 37 cases (28.5%) (Table 2). Thirty patients (23.1%) also required biliary reconstruction in addition to their resection.

Of the 126 resections performed where the postoperative survival was greater than 24 hours, postoperative intra-abdominal sepsis occurred in 36 patients (28.6%). By means of univariate analysis using Student's t-test and the chi-square test, we were able to identify several clinical and biochemical variables significantly associated with the development of posthepatectomy intra-abdominal infection (Tables 3 and 4). However, a stepwise discriminant analysis disclosed that the only significant factors related independently to the development of postoperative intra-abdominal infection were a diagnosis of either trauma or cholangiocarcinoma, or if reoperation was required during the early postoperative period to control hemorrhage. If one excludes the 19 patients who presented with trauma, and the 27 cases of cholangiocarcinoma, then in only twelve of 80 cases (15%) did intra-abdominal sepsis develop. A statistical analysis of clinical and laboratory values of these 80 patients now reveals that the only independent variable statistically associated with the development of sepsis is the need to reoperate to control postoperative hemorrhage.

TABLE 1. *Indications for Hepatic Resection and Percentage of Patients Developing Posthepatectomy Intra-abdominal Sepsis*

Indications for Hepatic Resection	No. of Patients	Infected	% Infected
Malignant			
Primary			
Cholangiocarcinoma	27	14	51.9
Hepatocellular carcinoma	20	6	30.0
Other primary	3	0	
Secondary	34	4	11.8
Benign			
Haemangioma	7	0	
Focal nodular hyperplasia	5	0	
Hepatic adenoma	4	0	
Other	7	2	28.6
Trauma	19	10	52.6
Total	126	36	28.6

Before 1984, the preferred approach in this unit for the management of posthepatectomy intra-abdominal infection was reoperation. As available diagnostic imaging techniques improved and confidence was gained with methods of percutaneous drainage, nonoperative drainage of suspected postoperative intra-abdominal abscesses rapidly became the procedure of choice (Table 5).

Of the 36 patients who developed postoperative intra-abdominal sepsis, 16 were treated by reoperation and 14 underwent percutaneous drainage of the septic focus. Two of the 14 patients (14.3%) who were initially managed by percutaneous drainage eventually died despite having a laparotomy for persistent sepsis. One of these two patients initially improved after percutaneous drainage of an infected collection of bile-stained fluid 14 days after extended right hepatectomy and hepaticojejunostomy for cholangiocarcinoma, but required formal reoperation 11 days later. It was discovered that the hepaticojejunostomy had broken down and required refashioning. This patient ultimately died 33 days after hepatic resection due to per-

TABLE 2. *Resections Performed in 126 Patients in Whom Postoperative Survival was Greater than 24 Hours, and Percentage of Patients Who Developed Posthepatectomy Intra-abdominal Sepsis*

Surgical Procedure	No. of Patients	Infected	% Infected
Extended right hepatectomy	28	10	35.7
Extended left hepatectomy	7	3	42.9
Right hepatectomy	40	14	35.0
Left hepatectomy	14	3	21.4
Left lateral hepatectomy	9	0	
Segmental hepatectomy	28	6	21.4
Total	126	36	28.6

TABLE 3. *Variables Assessed for Association with Posthepatectomy Intra-abdominal Sepsis by Students' t-test*

Variables	No. of Patients Infected	No. of Patients Not Infected
Age (years)	39.3 ± 2.7	44.6 ± 1.7
Preoperative stay (days)	9.8 ± 1.2	7.8 ± 0.8
Postoperative stay (days)	41.2 ± 2.6	16.9 ± 1.8*
Albumin (g/l)	31.4 ± 1.5	40.2 ± 1.0*
Prothrombin time (seconds)	9.9 ± 0.7	13.4 ± 0.5*
Total bilirubin (μmol/l)	109.4 ± 21.7	43.1 ± 14.2
Aspartate aminotransferase (iu/l)	55.9 ± 14.5	74.0 ± 9.6
Alkaline phosphatase (iu/l)	44.1 ± 70.6	276.4 ± 46.8
Creatinine (μmol/l)	70.3 ± 5.2	81.3 ± 3.5
Urea (mmol/l)	3.96 ± 0.45	5.28 ± 0.29*
Operative time (minutes)	240 ± 21	262 ± 14
Operative transfusion (units)	12.7 ± 1.8	9.4 ± 1.1

* $p < 0.05$.

TABLE 5. *Initial Method of Drainage of Posthepatectomy Intra-abdominal Infection*

Year	Percutaneous Drainage	Operative Drainage	Spontaneous Drainage
1979	0	1	0
1980	0	4	1
1981	0	3	1
1982	1	2	1
1983	0	4	1
1984	3	1	0
1985	2	1	2
1986	3	0	0
1987	5	0	0
Total	14	16	6

sistent sepsis. The second patient who died after initial percutaneous drainage had persistent clinical sepsis after a right hepatectomy for polycystic disease of the liver. A percutaneous drain was inserted into a subphrenic fluid collection and drained pus, which grew a pure growth of *Escherichia coli*. Despite this, she remained septic; reoperation was performed, but a septic focus could not be found and she died soon afterwards. Postmortem examination disclosed diffuse intrahepatic abscesses in the residual cyst cavities.

Generally, complications experienced with the percutaneous drainage technique were few, and in four patients (28.6%), included the need to reposition the catheter or perform a repeat percutaneous puncture before complete resolution of the infection could occur. Three patients developed an empyema after percutaneous drainage of a subphrenic abscess, most probably due to transgression of the pleural space by the catheter with subsequent contamination. Two of these patients had complete resolution of the empyema by chest tube drainage alone. One patient required a minor rib resection before the infection resolved.

Of the 16 patients treated by reoperation, six ultimately died within 30 days. Reoperation was complicated in most cases by the presence of dense vascular adhesions increasing the complexity of the surgical procedure and making hemostasis difficult to achieve. Two of the patients who were submitted to reoperation required a further operation to control hemorrhage after the drainage procedure, and both of these ultimately died. Another patient had recurrent septic symptoms after operative drainage of an infected perihepatic fluid collection; a second fluid collection was identified and was treated on this occasion by percutaneous drainage, with no further recurrence.

Spontaneous drainage of an infected intra-abdominal fluid collection occurred in six patients. Spontaneous drainage was usually manifested as discharge of purulent material through the wound or a drain track, with rapid resolution of systemic symptoms. One patient who had been repeatedly investigated for postoperative intra-abdominal sepsis suddenly drained a pelvic abscess *per rectum* with complete resolution of his pyrexia.

Detailed aerobic and anaerobic culture of the drainage fluids disclosed the presence of multiple strains of bacteria in 18 of the 36 patients with posthepatectomy intra-abdominal sepsis. The most frequent pathogens isolated were *Streptococcus faecalis (Enterococcus)*, *E.coli*, *Staphylococcus epidermidis*, and *Staphylococcus aureus* (Table 6). In four of six patients with positive preoperative bile cultures obtained at the time of percutaneous biliary decompression, the postoperative intra-abdominal infection included the same bacteria.

In six other patients, clinical signs and symptoms strongly suggestive of a post-operative intra-abdominal

TABLE 4. *Variables Significantly Associated with Posthepatectomy Intra-abdominal Sepsis by chi-square Analysis, $p < 0.05$*

Reoperation for hemorrhage*
Cholangiocarcinoma*
Trauma*
Preoperative percutaneous biliary decompression
Extensive hepatic resection (EHL + RH)
Transfusion ≥ 10 units
Biliary reconstruction

* Variables independently associated with sepsis after multivariable analysis.

TABLE 6. *Bacterial Isolates from Posthepatectomy Intra-abdominal Infections*

Streptococcus faecalis	14
Escherichia coli	11
Staphylococcus epidermidis	10
Staphylococcus aureus	9
Pseudomonas sp.	7
Klebsiella sp.	5
Other	9
Total	64

infection developed and were found to have perihepatic fluid collections by imaging. One patient underwent reoperation and five patients had percutaneous drainage, with resolution of the symptoms occurring in all, but no bacteria were isolated after culture of the fluid. These patients had invariably been on broad spectrum antibiotics at the time of percutaneous drainage but had persistent symptoms of sepsis that had been attributed to the fluid collection.

Discussion

Our data suggest that posthepatectomy intra-abdominal sepsis is a common clinical problem that can be effectively managed by percutaneous drainage in most cases. Of 126 cases in which postoperative survival was greater than 24 hours, the infection rate was 28.6%, higher than in the series reported by Fortner[1] (20.4%), Thompson[2] (16.7%), or Iwatsuki et al.[6] (8%). This difference may possibly be due to a different patient population, particularly as our stepwise discriminant analysis suggests postoperative intra-abdominal infection to be significantly associated with a diagnosis of cholangiocarcinoma or trauma. Twenty-seven of our cases (20.8%) of hepatic resection were for a diagnosis of cholangiocarcinoma, and 22 for trauma (16.9%), which is a considerably different population from that of other previous reports. Although Iwatsuki[6] includes trauma in his series, he reports only three cases (1.2%), and none of the reported series have more than 6.5% of the resections performed for cholangion carcinoma.[2] When these two high-risk groups are removed from our series, the incidence of postoperative intra-abdominal infection is 15% (twelve of 80 patients), which is similar to that reported by other authors, including the Eastern series reported by Yanaga,[3] where the infection rate was 12.8%.

Several investigators have suggested that the large residual cavity remaining after extensive resection and the presence of an ischemic margin of liver tissue at the resection line creates a predisposition to the development of infection.[1,3] Experimental work suggests that the presence of blood or bile in the peritoneal cavity may impair the normal host defense mechanisms,[4,5] and that hyperbilirubinemia may cause some impairment of lymphocyte function.[10] In this respect, the finding that patients with cholangiocarcinoma are at an increased risk for postoperative intra-abdominal sepsis may be related to prolonged preoperative hyperbilirubinemia, extensive hepatic resection with a large transfusion requirement, and the hazard of a biliary-enteric anastomosis frequently performed in the presence of infected bile. In patients subjected to preoperative percutaneous biliary decompression, bacterial colonization of the bile may offset any gains from a lowered serum bilirubin level.[11,12] Patients with hepatic trauma may be at increased risk for postoperative sepsis because of the presence of extensive tissue devitalization from the injury, with associated hypotension and the need for multiple transfusions and, frequently, injury to other organs.[13] In our series, 78.9% of trauma patients (15 of 19 patients) had had a prior laparotomy and attempted control of hemorrhage, often with insertion of abdominal packs, before transfer to this unit for management. The need for multiple operations and the possibility that sepsis was present before the hepatic resection are partially responsible for this increased infection rate.

Patients requiring a second operation for control of hemorrhage during the early posthepatectomy period were also at increased risk of postoperative sepsis. These patients had often had an extensive hepatic resection, with a postoperative coagulopathy contributing to the bleeding problem. Continued oozing after the second operation may have contributed to the development of a perihepatic abscess.

In the posthepatectomy patient, the diagnosis of intra-abdominal sepsis is frequently difficult to make. It is usually considered in cases where there is persistent postoperative pyrexia or unexplained deterioration in the clinical condition, including hepatic failure.[3,14] When faced with a patient with possible posthepatectomy intra-abdominal sepsis, we generally use ultrasonography as the first method to examine for evidence of a potentially septic focus in the abdomen. If the scan is negative and there is persistent suspicion of sepsis, we then obtain a CT scan, as this may provide a better assessment of the perihepatic space. If a fluid collection is identified by either imaging technique, we then proceed to percutaneous drainage. In the cases managed in this manner, 89.5% recovered (17 of 19 patients), and in 73.4% (14 of 19 patients) the fluid proved to be infected on culture. The prompt clinical improvement that occurred in those patients who had a sterile culture suggests that the source of the symptoms lay in the fluid collection. The symptoms may be explained by the presence of tissue breakdown products that cause a pyrogenic reaction,[6] or, although the fluid may indeed have been infected, but high circulating levels of antibiotics resulted in a spurious result.

Reoperation for intra-abdominal sepsis is a technically demanding procedure that was often poorly tolerated by already debilitated patients. Although not statistically significant, the worse survival rate in the reoperation group (62.5%) as compared to the percutaneous drainage group (85.7%) suggests that, where appropriate, one should initially attempt percutaneous intervention for all posthepatectomy intra-abdominal abscesses; this is in concordance with the views of others [7,8,15]. Presently, we consider laparotomy for posthepatectomy intra-abdominal sepsis only if there are signs of significant spreading peritonitis or if there is some other additional indication for reoperation.

Summary

Review of clinical data for an unselected group of patients treated at one institution over an 8-year period has disclosed a 28.6% incidence of posthepatectomy intra-abdominal infection. Factors significantly associated with the development of intra-abdominal infection were a diagnosis of either trauma or cholangiocarcinoma, or the need for reoperation to control bleeding during the early postoperative period. Percutaneous drainage for posthepatectomy intra-abdominal sepsis is successful in most cases of localized infection, and has become our preferred treatment modality in the septic posthepatectomy patient.

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