Etiological Factors in Fatal Complications Following Operations Upon the Biliary Tract *

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WIDE ACCEPTANCE of surgical therapy for nonmalignant disease of the biliary tract has come about because of the safety and ease with which it is accomplished as well as the satisfactory relief of symptoms and interruption of the pathologic processes involved. During the 95 years that have elapsed since John S. Bobbs [1] (June 15, 1867) performed a cholecystotomy, removing some 50 gallstones and providing immediate and dramatic relief to the patient, an ever-increasing proportion of those with biliary calculi have been benefited by surgery. Cholecystectomy and choledochotomy had become established procedures by 1890, albeit with too few reports available upon which to determine the risk involved. Between 1900 and 1910, meager and sporadic accounts lead to an estimated mortality rate of 10 to 15 per cent for operations upon the biliary tract. Both the profession and patients sought to avoid surgery except in advanced and critical phases of the disease.

In 1934, Heuer [6] reviewed 21 reports from representative American and European hospitals published between 1923 and 1932 and in some instances relating to experiences extending from before 1900. The over-all mortality rate of 36,623 cases was 6.6 per cent. An analysis of information available concerning the 2,453 deaths led him to conclude that they were in large part due to:

1. Far-advanced biliary tract disease and liver insufficiency
2. Errors in surgical management
3. Pulmonary complications usually associated with anesthesia
4. Pathologic changes involving the cardiovascular-renal systems
5. A small proportion (15%) were attributed to miscellaneous and undetermined conditions.

Since 1932, 5,797 patients have been operated upon for nonmalignant disease of the biliary tract on the pavilion services of The New York Hospital-Cornell Medical Center. This disease and its sequelae now constitute one of the most frequent indications for operation in this center.

In 1952, Glenn and Hays [5] reported a detailed study of 63 fatalities following operations for nonmalignant disease of the biliary tract upon 3,439 patients at The New York Hospital-Cornell Medical Center from September 1, 1932 through August 31, 1950 (Fig. 1). During this 18-year period two trends became apparent. First, the mortality rate was decreasing, second, the relative distribution of causes of death was changing appreciably. There had been a decrease in the proportion of deaths attributed to hemorrhage, shock, and intra-abdominal infection (excluding the biliary tract) and an increase in the proportion of those due to degenerative disease processes. Pulmonary complications as a cause of death remained constant. The authors emphasized their observation that 30 per cent of deaths in the cases studied were attributed to hepatic infection, cirrhosis or

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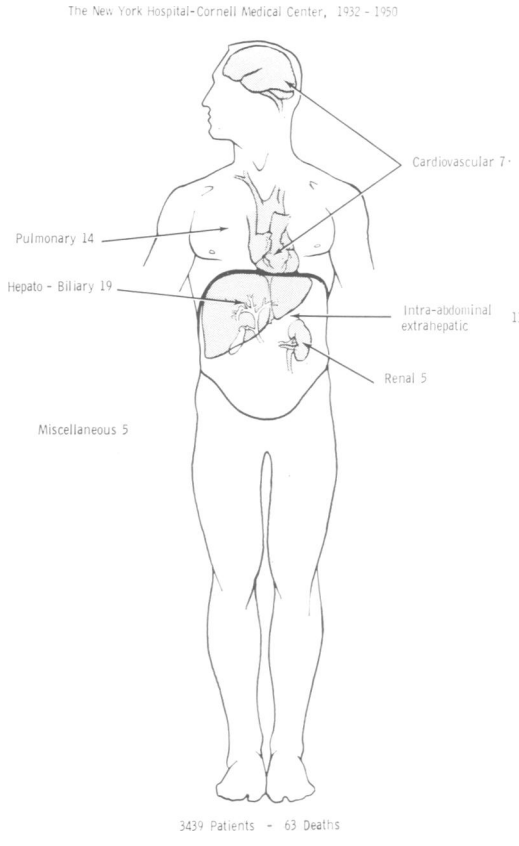

FIGURE 1.

necrosis. They also attached importance to their finding evidence of biliary cirrhosis in 52 of the 63 fatalities. These liver changes were considered to be related directly to 1) duration of nonmalignant biliary tract disease; and 2) the necessity of multiple operations upon the biliary tract.

The present report includes a discussion of the causes of death following surgery for nonmalignant disease of the biliary tract on an additional 2,358 patients with 39 postoperative deaths that were treated at The New York Hospital-Cornell Medical Center from September 1, 1950 through August 31, 1962 (Fig. 2). These are discussed in conjunction with the over-all experience of 30 years (1932–1962) (Fig 3). The objective is to focus attention upon conditions and circumstances common to those who develop fatal complications so that suitable measures may be taken to decrease the hazard they present. Concomitantly it becomes evident that selection and adaptation of the surgical procedure to the individual patient according to the particular situation reduces the risk.[8]

Clinical Material

The total number of operative cases and the types of operation employed are listed in Table 1. The over-all mortality for the 11-year period during which 2,358 patients were operated upon was 1.7 per cent. Of the 39 postoperative deaths, 24 were women and 15 men. These patients ranged in age from 31 years to 89 years with an average age of 68.2 years. Complete postmortem examination was performed in 22 patients (56.4%).

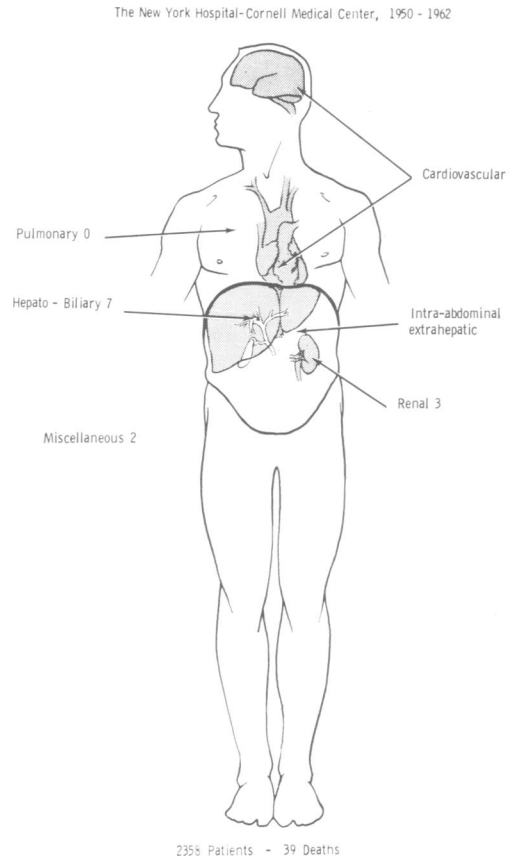

FIGURE 2.

TABLE 1. *Total Operative Cases and Postoperative Deaths in Nonmalignant Biliary Tract Disease*

Operations Performed	Operations No.	Operations Total	Deaths No.	Deaths Total	Mortality %	Mortality Total
Cholecystectomy for						
Acute cholecystitis	266		6		2.3	
Chronic cholecystitis	1,444		4		0.3	
		1,710		10		0.6
Cholecystostomy	48	48	6	6	12.5	12.5
Choledochotomy						
Plus cholecystectomy	388		11		2.8	
Without cholecystectomy	139		3		2.3	
		527		14		2.7
Miscellaneous procedures*	73	73	9	9		12.3
Totals		2,358		39		1.7

* Postoperative deaths occurred following choledocholithotomy and repair cholecystoduodenal fistula, choledocholithotomy and repair cholecystocolic fistula, cholecystectomy and drainage of common duct, cholelithotomy and cholecystenterostomy, cholecystostomy and drainage of common duct, choledochoenterostomy.

Elective cholecystectomy for chronic cholecystitis is the most common operative procedure performed for nonmalignant biliary tract disease. Four of 1,444 patients undergoing elective cholecystectomy died in the immediate postoperative period. This constitutes an operative mortality of 0.3 per cent. Since it appears that at the present time the most effective means of lowering the mortality rate for the surgical treatment of calculous disease of the biliary tract lies in the performance of elective cholecystectomy prior to the onset of late sequelae and complications, these 4 deaths will be examined in detail.

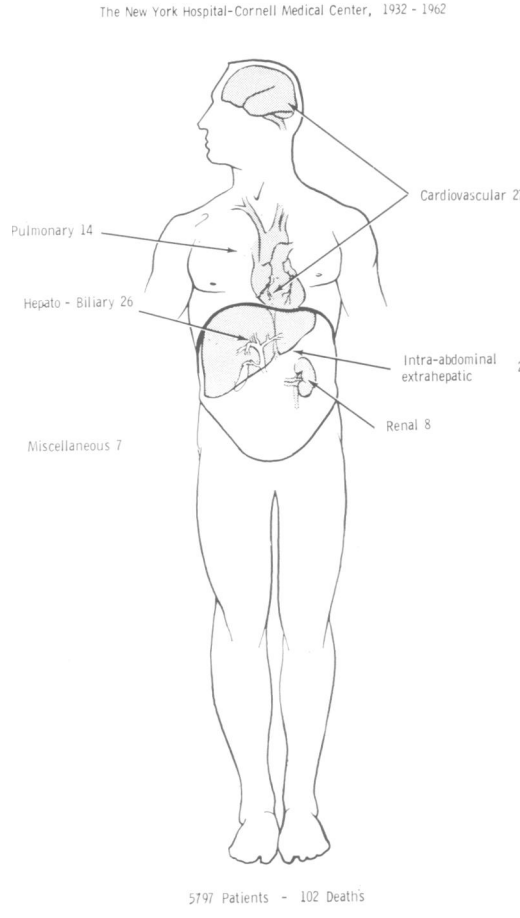

FIGURE 3.

Case Reports

E. C. NYH 879 935. A 59-year-old white man was admitted because of a 2-year history of recurrent attacks of right upper quadrant and epigastric pain precipitated by the ingestion of fried foods. Past history was significant in that the patient had syphilis at age 15 for which he received "multiple injections." A review of systems was noncontributory. Specifically, the patient denied any symptoms of cardiovascular disease. On admission the blood pressure was 104/70 and the pulse 86. Abdominal examination revealed minimal right upper quadrant tenderness on deep palpation. Examination of the heart revealed no enlargement or murmurs. There were no stigmata

of lues. Laboratory data included a normal urinalysis, blood count, blood urea nitrogen and prothrombin time. The electrocardiogram was interpreted as normal.

Four days following an uneventful cholecystectomy, the patient developed a left hemiparesis and aphasia. Electrocardiogram at this time revealed changes consistent with an anterior myocardial infarction. Spinal fluid examination was negative. The patient was thought to have a right middle cerebral artery embolus secondary to a mural thrombus and myocardial infarction. He expired on the 7th postoperative day and 3 days after the onset of hemiparesis. Postmortem examination was not performed.

Comment: This postoperative death is considered unavoidable. There were no factors in the preoperative evaluation to suggest cardiovascular disease.

R. B. NYH 623 940. A 77-year-old white woman was admitted to the medical service because of a 9-month history of anorexia, 60-pound weight loss and increasing constipation. The patient also complained of intermittent precordial pain, dyspnea, orthopnea and ankle edema. On admission the blood pressure was 248/140, and the pulse 90. The heart was moderately enlarged and a loud apical systolic murmur was heard. The liver was palpable 2.0 cm. below the costal margin. Urinalysis revealed 3+ albuminuria and intravenous pyelography demonstrated a nonfunctioning left kidney and a hydronephrotic right kidney. The blood urea nitrogen was 22 mg%. Barium enema demonstrated diverticulosis and oral cholecystogram, cholelithiasis. Following appropriate preoperative preparation including digitalis therapy, the patient underwent cholecystectomy and appendectomy. Nine hours postoperatively she developed acute pulmonary edema and expired. Postmortem examination was not performed.

Comment: The combination of severe hypertension, coronary artery disease with angina pectoris, congestive failure and markedly impaired renal function rendered this patient a poor risk for any surgical operation. Operative mortality in patients such as this one can be reduced by doing the least burdensome operative procedure to meet the immediate circumstances. In this patient, cholecystostomy under local anesthesia might have resulted in a more favorable outcome.

A. S. NYH 843 386. A 54-year-old Negro woman with hypertension was admitted to the hospital for evaluation of an aneurysm of the right renal artery discovered on an intravenous pyelogram. The patient also had a history of fatty food intolerance and intermittent episodes of upper abdominal pain. Oral cholecystogram demonstrated cholelithiasis.

Following extensive urologic evaluation the patient underwent resection of the right renal artery aneurysm and a cholecystectomy was also done. Postoperatively, she developed a fever of 40° C. and had evidence of generalized peritonitis. Exploratory laparotomy was performed on the second postoperative day. During this procedure the patient sustained a cardiac arrest and expired. Postmortem examination revealed hypertensive arteriosclerotic cardiovascular disease and multiple infarcts of the right kidney. No explanation for the peritoneal signs was found. Material for culture from the peritoneum failed to grow out organisms.

C. S. NYH 779 116. A 57-year-old white woman was admitted because of epigastric pain and weight loss of 2-months' duration. Gastrointestinal series revealed a carcinoma of the antrum of the stomach. A subtotal gastrectomy with splenectomy and omentectomy was performed. In addition, the patient had hydrops of the gallbladder with a stone impacted in its ampulla for which a cholecystectomy was also performed. The patient expired on the 20th postoperative day due to an acute myocardial infarction. Postmortem examination was not done.

Comment: These last two patients illustrate a problem occasionally encountered at the operating table, namely the finding of cholelithiasis during the course of an operation performed for abdominal diseases not associated primarily with the biliary tract. As a general rule, it is inadvisable to perform an *incidental* cholecystectomy. However, in certain situations, for example, acute cholecystitis and cystic duct obstruction, it may be necessary to perform a cholecystostomy. In situations where gallstones are not obstructing the cystic duct and there is no evidence of active inflammation, it appears advisable not to perform cholecystectomy.

Cholecystectomy for acute cholecystitis was performed on 266 patients with six

postoperative deaths, a mortality of 2.3 per cent. In three of these patients, the gallbladder had perforated prior to operation.

Cholecystostomy was performed on 48 patients with 6 postoperative deaths, a mortality of 12.5 per cent. This high mortality is a reflection of the poor operative risk of the patients for whom this operation is reserved.

Three hundred and eighty-eight patients underwent cholecystectomy plus choledochotomy for either chronic or acute cholecystitis and evidence of common duct obstruction. There were 11 postoperative deaths, a mortality of 2.8 per cent. Choledochotomy alone was performed on 139 patients, all of whom had undergone cholecystectomy in the past. There were three postoperative deaths, a mortality of 2.2 per cent. Cholecystectomy had been performed in these three patients, 4, 6, and 10 years prior to choledochotomy.

Seventy-three patients underwent a variety of procedures on the biliary tract. Nine postoperative deaths occurred in this group of 73 patients, a mortality of 12.3 per cent.

Indication for Operation. The indications for operation in the 39 patients in whom postoperative deaths occurred are listed in Table 2. The majority of these patients (56.4%) presented with acute cholecystitis with and without choledocholithiasis. Ten patients (25.6%) had chronic cholecystitis with and without choledocholithiasis. Three patients, postcholecystectomy, were operated upon for choledocholithiasis. Choledocholithiasis and cholecystoduodenal fistula were the indications for operation in two patients and choledocholithiasis and cholecystocolic fistula in one patient. Postoperative stricture of the choledochus was the indication for operation in the remaining patient.

Types of Fatality. The 39 postoperative deaths are classified in Table 3 according to the primary cause of death based on clinical and autopsy findings. Cardiovascular-renal disease, manifested as acute coronary occlusion, congestive heart failure, cardiac arrest, renal insufficiency, cerebrovascular accident and pulmonary arteritis accounted for 23 of the 39 postoperative deaths (58.9%). Three illustrative case reports follow.

TABLE 2. *Indications for Surgical Intervention in 39 Cases of Fatality Following Biliary Tract Surgery for Benign Disease*

	No.	Totals
Acute cholecystitis	13	
Acute cholecystitis with choledocholithiasis	9	22
Chronic cholecystitis	4	
Chronic cholecystitis with choledocholithiasis	6	10
Postoperative stricture of the choledochus	1	
Choledocholithiasis (previous cholecystectomy)	3	
Choledocholithiasis and choledochoduodenal fistula	2	
Choledocholithiasis and cholecystocolic fistula	1	7
Total		39

E. M. NYH 659 778. A 75-year-old housewife was admitted because of abdominal pain. Twenty years prior to admission, she noted the onset of fatty food intolerance and a cholecystogram 15 years before admission demonstrated cholelithiasis.

On physical examination at the time of admission the temperature was 38.5° C., the pulse 100, and the blood pressure 180/80. The heart was enlarged to the left of the mid-clavicular line and there was a Grade 2 apical systolic murmur. Abdominal examination revealed direct and rebound tenderness in the right upper quadrant. The gallbladder was not palpable. Intravenous cholangiography was performed and the gallbladder was not visualized. Electrocardiogram revealed changes consistent with coronary artery disease.

Five days following cholecystectomy, the patient complained of severe precordial pain. Electrocardiogram indicated an anterior myocardial infarction. The patient was kept on bed rest for a period of five weeks. Two hours after the pa-

TABLE 3. *Causes of Death Following Biliary Tract Surgery for Nonmalignant Disease (Based on Clinical and Autopsy Findings)*

Cause of death	No. Deaths	Totals
Cardiovascular-renal disease		23
Acute coronary occlusion	9	
Congestive heart failure	7	
Renal insufficiency	3	
Cardiac arrest	2	
Acute necrotizing pulmonary arteritis	1	
Cerebrovascular accident	1	
Hepato-biliary disease		7
Hepatic cirrhosis	5	
Liver abscesses	2	
Infection (Intra-abdominal, extrahepatic)		7
Subhepatic abscess	3	
Generalized peritonitis	1	
Pseudomembranous enterocolitis	3	
Miscellaneous*		2

* Carcinoma of the cecum with liver metastasis. Gastro-intestinal hemorrhage secondary to allegic purpura.

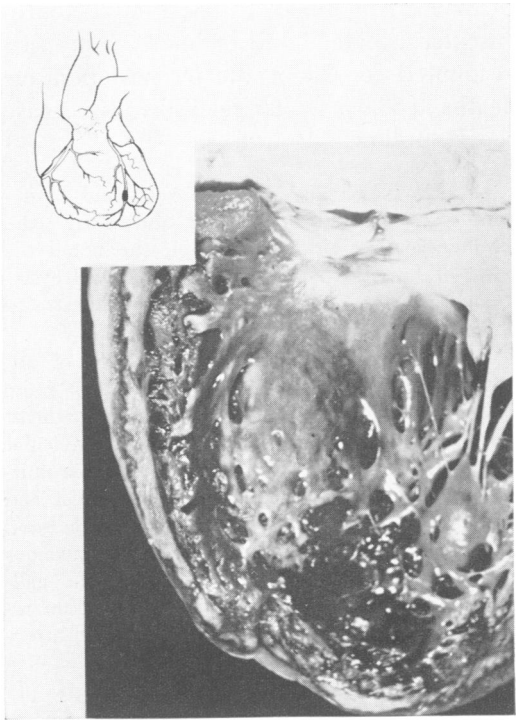

FIG. 4. Myocardial infarction in a 75-year-old mother.

tient was first allowed out of bed she expired suddenly.

On postmortem examination there was complete occlusion of the left anterior descending branch of the left coronary artery near its ostium by an atheromatous plaque. At the base of the lateral wall of the left ventricle there was an area of white fibrous scarring of 4.0 cm. in diameter (Fig. 4).

V. B. NYH 623 990. A 77-year-old widow was admitted on August 23, 1952, because of severe right upper quadrant abdominal pain of 24 hours' duration associated with nausea and vomiting. Physical examination revealed blood pressure of 160/85, pulse 90 and temperature 38.4° C. The heart was moderately enlarged and an apical systolic murmur was noted. On abdominal examination there was moderate right upper quadrant tenderness. The gallbladder was not palpable. Laboratory studies included normal electrocardiogram and serum electrolytes. The blood urea nitrogen was 12 mg%.

On the third hospital day, an acutely inflamed gallbladder was removed under general anesthesia. On the third postoperative day, mental confusion and oliguria were noted. The blood urea nitrogen was 52 mg.%. Despite appropriate and vigorous measures the patient remained oliguric and ex-

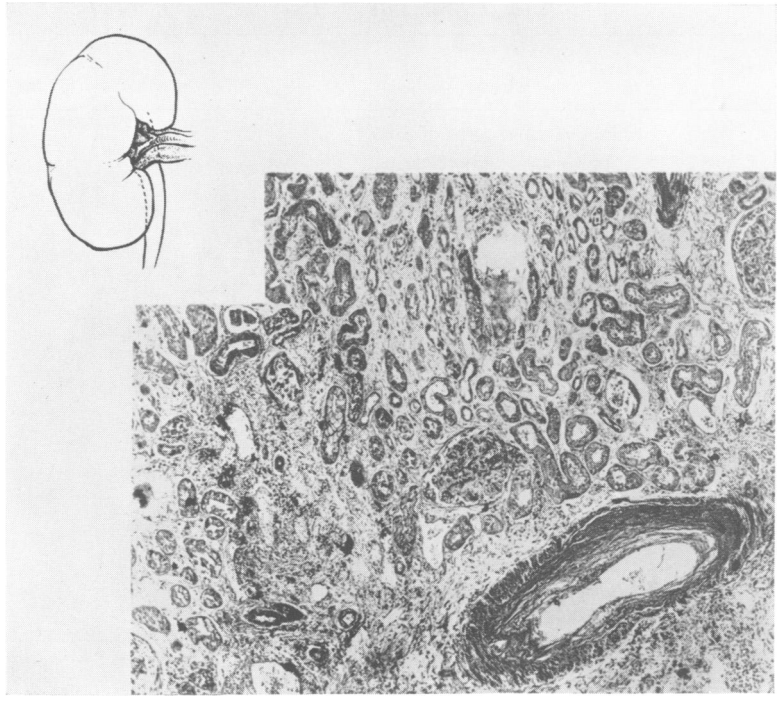

FIG. 5. Pyelonephritis with marked arteriolar sclerosis in a 77-year-old widow.

pired on the tenth postoperative day at which time her blood urea nitrogen was 190 mg.%.

Postmortem examination revealed bronchopneumonia and hypertensive and arteriosclerotic cardiovascular disease. Examination of the kidneys demonstrated acute and chronic pyelonephritis with advanced arteriolar nephrosclerosis and glomerularsclerosis (Fig. 5).

E. F. NYH 756 408. A 76-year-old housewife was admitted on December 23, 1956, because of an intertrochanteric fracture of the left hip. The patient denied any cardiovascular or gastrointestinal complaints.

Physical examination on admission revealed a blood pressure of 160/90 and an irregular pulse of 108. Coarse inspiratory rales were audible throughout both lung fields. The heart was not enlarged and a moderately loud systolic murmur was audible at the apex. Abdominal examination was unremarkable. The left leg exhibited 1½ inches of shortening and was maintained in a position of external rotation.

Two days following closed reduction and internal fixation of the hip fracture the patient developed abdominal pain, nausea, vomiting and fever of 40.5° C. Physical examination disclosed slight icterus and a tender, palpably enlarged gallbladder. Under local anesthesia, cholecystostomy and choledocholithotomy were performed. The patient did well until the 7th postoperative day when she suddenly became comatose and developed a right hemiparesis. Eight days later the patient expired.

Postmortem examination revealed generalized cerebral arterial sclerosis with infarction of the left parietal lobe of the brain (Fig. 6).

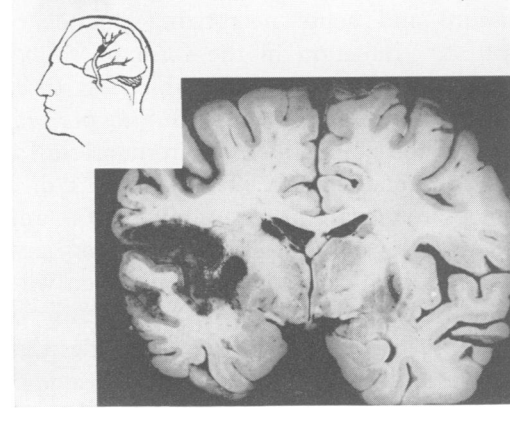

FIG. 6. Cerebral infarction, left parietal lobe, in a 76-year-old housewife and mother, with advanced arteriosclerosis.

TABLE 4. *Deaths (Following Biliary Tract Surgery) with Complete Postmortem Examinations*

Cause of death	No. Patients	Totals
Cardiovascular-renal disease		12
Acute coronary occlusion	4	
Congestive heart failure	2	
Cardiac arrest	1	
Cerebrovascular accident	1	
Acute necrotizing pulmonary arteritis	1	
Renal insufficiency	3	
Hepato-biliary disease		4
Hepatic cirrhosis	2	
Liver abscesses	2	
Infection (Intra-abdominal, extrahepatic)		4
Subhepatic abscess	2	
Generalized peritonitis	1	
Pseudomembranous enterocolitis	1	
Miscellaneous		2
Carcinoma cecum with liver metastasis	1	
Gastro-intestinal hemorrhage due to allergic purpura	1	

Primary hepatic disease, five patients with cirrhosis and two with multiple liver abscesses, was the next most frequent cause of death. These seven patients accounted for 17.9 per cent of the postoperative deaths. Although hepatic cirrhosis was present in 10 patients, it appeared to be the primary cause of death in only five patients. Two patients with cirrhosis died from coronary occlusion and one each from renal insufficiency, congestive heart failure and acute necrotizing pulmonary arteritis. Infection in the form of subhepatic abscess was responsible for three deaths and bile peritonitis due to perforation of the gallbladder was responsible for an additional fatality. Three patients died of pseudomembranous enterocolitis and one from a gastro-intestinal hemorrhage and another from carcinoma of the cecum with liver metastasis. Table 4 lists the cause of death in the 22 postoperative fatalities that had complete postmortem examination.

Discussion

Trends have changed over the past 40 years with respect to types of fatality following surgery for nonmalignant biliary tract disease. Heuer's review, in 1934, of 2,453 fatalities following biliary tract surgery indicates that the major problems in the early part of this century were related to advanced disease, surgical procedures *per se*, and postoperative pulmonary complications. Glenn and Hays in 1952 reporting on the causes of death in 63 postoperative fatalities that occurred among 3,439 patients in the period 1932–1950, stress the importance of hepatic insufficiency associated with infection, cirrhosis and necrosis as the major cause of postoperative deaths. This present study, which is concerned with 39 postoperative deaths that occurred in the period September 1, 1950 through August 31, 1962, indicates that the principal cause of death is now cardiovascular disease.

There are several factors contributing to trends regarding the types of fatalities that occur following biliary tract surgery. Perhaps the most important factor is the advancing age of the general population. Table 5 lists the incidence of hypertension, diabetes mellitus, arteriosclerotic heart dis-

ease and generalized arteriosclerosis present in the 39 postoperative deaths. Advancing age, *per se*, should not preclude surgical treatment for calculous disease of the biliary tract. However, in these patients preoperative evaluation of cardiac, pulmonary and renal function is mandatory. The selection of anesthesia and the operative procedure to be employed must be based in part on the patient's general condition, as well as the pathology of the biliary tract for which the surgery is undertaken.

The declining role of hepatic disease as a cause of death following biliary tract surgery is most interesting. It is probably related to the wide acceptance of surgical therapy for the treatment of the early stages of biliary tract disease. The concepts of *liver death* as reported by Heyd,[7] in 1924 and the clinical syndrome of hepatorenal failure as described by Heyd and later Boyce[2] and others[3, 4, 9, 10] are now questioned.

The three postoperative deaths attributed to renal insufficiency occurred in patients with 1) acute and chronic glomerulonephritis plus intercapillary glomerulosclerosis; 2) arteriolar nephrosclerosis; and 3) renal tuberculosis and thrombosed renal arteries.

Infection continues to be a major problem in biliary tract surgery as is evident by three deaths attributable to subhepatic abscess, one death due to bile peritonitis and three deaths attributable to pseudomembranous enterocolitis. Antimicrobial therapy has been most important in the treatment of biliary tract infections, particularly cholangitis and liver abscess. The use of antibiotics is not without danger, however, and contributed to the occurrence and severity of pseudomembranous enterocolitis.

Summary

An analysis of 39 deaths that followed surgery for nonmalignant disease of the biliary tract among 2,358 patients over a 12-year period (1950–1962) at The New York Hospital-Cornell Medical Center presented the major causes for death as cardiovascular disease and infection. This experience is compared to a study of 63 postoperative deaths that occurred among 3,439 patients following operation for the same disease over a period of 18-years (1932–1950) in The New York Hospital-Cornell Medical Center. The major causes for death of this group were hepatic infection, cirrhosis and pulmonary disease. The over-all mortality rates were 1.8 per cent for the first 18 years and 1.7 per cent for the more recent period. Over the 30-year period, there has been an increase in the proportion of patients 65 years of age and older. The incidence of degenerative diseases in the elderly is higher and this appears to be the basis for the increase in the common causes for death. Infection and pulmonary disease are less frequent. More than ever before surgery for nonmalignant disease of the biliary tract is being accomplished with less risk and with greater ease from the patient's viewpoint. Reduction in time between the formation of calculi in the biliary tract and surgery should further reduce the risk since stones are present in almost 95 per cent of patients treated surgically for biliary tract disease.

TABLE 5. *Incidence of Hypertension, Diabetes Mellitus, Arteriosclerotic Heart Disease and Generalized Arteriosclerosis in 39 Deaths Following Biliary Tract Surgery for Nonmalignant Disease*

	No. Patients	%
Hypertension (greater than 140/90)	21	53.8
Diabetes mellitus	6	15.4
Arteriosclerotic heart disease	32	82.1
Mild (6)		
Moderate (17)		
Severe (9)		
Generalized arteriosclerosis	24	61.5
Moderate (14)		
Severe (10)		

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Discussion

Dr. Warren H. Cole (Chicago): I rise to discuss Frank Glenn's paper since I have had the opportunity of reading it. I want to commend Dr. Glenn on his low mortality rates, even though he is not happy with them. You will recall that in retrospect Dr. Glenn believes he would have had a lower mortality rate if he had chosen cholecystostomy rather than cholecystectomy in some of the cases.

Personally, I am convinced that the operative load is an important factor in the postoperative death when decrements or uncorrectible complications are present, meaning that a lighter load might be tolerated and not result in a fatality.

The big question is how severe should the complications be before the operation is contraindicated or should be changed to a lighter operation. There is, unfortunately, no categorical answer to this. You may recall that in Dr. Glenn's later series, the main cause of death was cardiovascular, whereas in the earlier series, hepatic disease and pulmonary diseases were major causes of death. The obvious explanation of this change in the cause of death seems definitely to be related to the fact that more patients in the late series belong in the older age group. And since old age leads to cardiovascular changes, the explanation seems quite valid.

I would like to emphasize certain points in identifying these warning signals which should be respected. In the first place, I am very apprehensive when the patient has a large cardiac shadow. That is a definite indication of some serious strain on the heart.

Also, I think we ought to try to detect evidence of coronary attacks of acute nature, particularly those occurring within three or four months of your proposed operation. I am sure that operations within three months of a coronary attack are dangerous, and often lead to death on the table. Unfortunately all these attacks are not necessarily accompanied by pain. The EKG will be helpful, particularly if there is a change, and a delay of a few days or perhaps a few weeks reveals a change back toward normal; a significant change in a short time indicates there has been a recent coronary attack. Obviously, those patients should not be subjected to operation less than three or four months after the attack.

Certain functional tests may be very helpful. I think we should always investigate by asking the patient about recent swelling of the ankles, dyspnea on exertion, and orthopnea; if these findings are present, the patient probably will not tolerate a serious operation. On such occasions we should subject the patient to a cholecystostomy rather than a cholecystectomy.

True enough, I do believe that we should try to evaluate the patient's operability more carefully, and often choose a lighter operation, such as cholecystostomy instead of cholecystectomy which Dr. Glenn has already advised. Thank you.

Dr. Robert S. Sparkman (Dallas): All of us are indebted to Dr. Glenn for having taught us so much through the years concerning the behavior and management of biliary tract disease.

My own experience in private practice comprises 407 operations for nonmalignant disease of the gallbladder and bile ducts with three deaths. These cases are classified as follows:

Procedure	Cases	Deaths
Cholecystectomy (duct explored in 25%)	344	2
Cholecystostomy	26	1
Choledochostomy alone	20	0
Duct Reconstruction	10	0
Removal of remnant	7	0
Mortality rate 0.74%	407	3