ORIGINAL ARTICLE

Cholecystectomy in Cardiothoracic Organ Transplant Recipients

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Objectives: To assess the risks associated with cholelithiasis and cholecystectomy in cardiothoracic organ transplant recipients at this hospital and to identify any differences with potential causal significance between the group with known gallstones and the transplant recipient group as a whole.

Design: Medical records survey.

Setting: Tertiary care university hospital.

Patients: Six hundred forty-five patients had cardiothoracic organ transplantation at this hospital between February 1, 1984, and May 31, 1996. Gallstones were detected in 37 (5.7%) of these patients and 32 patients underwent cholecystectomy, of which 29 operations were performed primarily for symptomatic gallstone disease. All cholecystectomies were performed after transplantation.

Main Outcome Measures: Mortality, morbidity, postoperative biliary disease.

Results: Patients with gallstones were significantly older than the transplant patient group as a whole (Student *t* test, $P=.001$); they were more likely to be female (χ^2 test, $P=.05$); and they had a higher body mass index (*t* test, $P=.001$). There were no significant differences in the maximum serum bilirubin level during the transplantation admission, incidence of diabetes mellitus, cholestyramine use, or cyclosporine dosage during the first 12 months after transplantation. Cholecystectomy was performed after a median 5-month symptomatic period, mostly by the minilaparotomy method. Forty-five percent of cholecystectomies were urgent or semi-urgent. One patient died of lung infection on the second postoperative day. The median postoperative stay was 3 days. At a median 33 months' follow-up, 4 patients have had further biliary problems (2 patients with common bile duct stones, 1 patient with intrahepatic stones, and 1 patient with biliary dyskinesia). Four other patients with asymptomatic gallstones who did not receive cholecystectomy have remained asymptomatic for between 15 and 67 months.

Conclusions: Cholecystectomy by the minilaparotomy or laparoscopic methods, with routine operative cholangiography, is the preferred treatment for symptomatic gallstones in cardiothoracic organ transplant recipients. Although the optimum management of asymptomatic gallstones in these patients remains unclear, our favorable experience with a policy of reserving cholecystectomy for symptomatic cases seems noteworthy.

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THE INCIDENCE of gallstone formation in heart transplant recipients is increased.[1-6] The use of cyclosporine, steroid-associated obesity or weight fluctuations, and diabetes mellitus[1] have all been suggested as contributing to gallstone formation in this transplantation group. Cyclosporine administration induced cholestasis with reduction of both bile flow[7,8] and bile acid secretion[7] in rats, although there was no correlation between mean blood cyclosporine levels and serum bilirubin or bile salt levels in a prospective study in human transplant recipients.[9] Other factors that might contribute to gallstone formation include older age, female sex, and use of cholesterol-lowering cholelithogenic drugs such as cholestyramine and clofibrate. In addition, both coronary artery disease and cystic fibrosis, for which cardiothoracic transplantation may be required, are associated with an increased incidence of gallstones.[10-12]

Cardiothoracic organ transplant recipients with gallstones also seem to be more liable to symptoms and complications caused by gallstones, compared with the general population.[4,6] In one study, symptoms caused by gallstones developed 2 ± 1.2 (SD) years after transplantation in 58% of patients with asymptomatic gallstones diagnosed before undergoing transplantation.[4] In a review of their own and all published cholecystectomies in cardiac transplant recipients, Begos et al[13] found that the mortality rate of urgent cholecystectomy was 44% (8 deaths in 18 patients). These results led to recommendations of regular screening ultrasonography for all transplant candidates and recipi-

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PATIENTS AND METHODS

This study was conducted at St Vincent's Hospital, Sydney, Australia, a teaching hospital affiliated with the University of New South Wales. Australia's first ongoing heart transplant program was established in 1984, and 645 patients received cardiothoracic organ transplantation at St Vincent's Hospital during the 12-year and 4-month period reviewed in this study. This number represents more than half of all cardiothoracic transplantations performed in Australia and New Zealand.[15]

The Cardiothoracic Transplant Data Base and general medical records for all patients who have undergone transplantation at St Vincent's Hospital were retrospectively reviewed by manual and computerized search, and all patients who had cholelithiasis, cholecystitis, cholecystectomy, or pancreatitis of any cause were identified. All transplant recipients are regularly and thoroughly followed up for long periods, and it is thus unlikely that any patients with symptomatic gallstone disease have not been identified.

The following data were collected for all patients who had undergone transplantation, including those who have also had gallbladder abnormalities: type of transplant, age and body mass index (obtained by dividing the weight [in kilograms] by the height [in meters] squared) at transplantation, sex, maximum serum bilirubin level during the transplantation admission, serum cholesterol levels, use of cholestyramine, presence of pretransplant or posttransplant diabetes mellitus, and cyclosporine dosage in the first year after transplantation. For patients who had gallbladder disease, the following additional information was collected: symptoms and signs of biliary disease; symptomatic period; maximum preoperative white blood cell count; maximum serum bilirubin, alkaline phosphatase, alanine transaminase, γ-glutamyltransferase, and serum albumin levels; and results of radiological biliary investigations. For patients who had cholecystectomy, interval from transplantation to cholecystectomy, operation type, American Society of Anesthesiologists grade of anesthetic risk, operative details, length of postoperative stay, operative morbidity and mortality, and condition and date at last follow-up were also recorded. Operations were classified as elective, urgent (operation within 48 hours), or semi-urgent (operation on next operating list for the surgeon involved). Follow-up information was obtained by postal and telephone inquiry with the patients themselves and their local physicians, and from the transplant and general medical records.

Comparison between the cholecystectomy and noncholecystectomy transplant recipients was made using the Student *t* test and the χ^2 test.

ents, with prophylactic cholecystectomy if gallstones are detected, even if the gallstones are clinically silent. Such a policy avoids the development of acute pathologic features in this immunosuppressed population, and avoids the need for urgent operation. Cholecystectomy before[3] or within approximately 6 months after transplantation[4,6,13,14] has been recommended for patients with gallstones detected by pretransplantation ultrasonographic examination.

This study was undertaken to determine the risks associated with cholelithiasis and cholecystectomy in cardiothoracic organ transplant recipients at this hospital. In addition, this study was performed to identify any differences with potential causal significance between the group with known gallstones and the transplant recipient group as a whole. Gallstones were less hazardous for transplant recipients in this study than in previously reported series, suggesting that a policy of reserving cholecystectomy for symptomatic patients may remain appropriate at this hospital.

RESULTS

In the 12-year and 4-month period from the first transplantation in February 1984 to the end of May 1996, a total of 645 patients have received thoracic transplants at St Vincent's Hospital. Of this total, 455 patients received heart transplants, 57 patients had heart and lung transplants, 70 had single lung transplants, and 63 had bilateral lung transplants.

Thirty-seven (5.7%) of the 645 transplant patients have had gallstones, of whom 30 patients have had cholecystectomy and 7 patients have not had cholecystectomy, for reasons detailed below. Thirty-two patients (5%) have had cholecystectomy, of whom 30 patients had gallstones and 2 patients did not have gallstones.

All cholecystectomies were performed after transplantation; no cholecystectomies were performed before transplantation on patients for the transplant waiting list. Twenty-nine patients had as their primary operation cholecystectomy for cholecystitis or biliary colic. These patients all had gallstones. Another 3 patients had cholecystectomy as part of other operations for more compelling indications and were excluded from further analysis.

The 37 patients with known gallstones were compared with the total population of patients who underwent transplantation to determine whether there were any significant differences between the 2 groups for factors that might influence gallstone formation. As given in **Table 1** and **Table 2**, patients with known gallstones were significantly older, significantly more likely to be women, and had a significantly higher body mass index. There was no significant difference between the 2 groups for the variables maximum serum bilirubin level during transplantation admission, incidence of diabetes mellitus, or cyclosporine dosage during the first 12 months after transplantation. Transplant recipients are often hypercholesterolemic because of cyclosporine use, corticosteroid use, or preexisting hypercholesterolemia in patients undergoing transplantation for ischemic heart disease, and 10% of all patients received the cholesterol-lowering but cholelithogenic drug cholestyramine, but there was no significant difference in the proportion of patients with known gallstones who received cholestyramine and the proportion of all transplant recipients who were given cholestyramine. Only a few patients received clofibrate, which is also cholelithogenic, and use of this drug was not analyzed.

Seven patients with known gallstones have not had cholecystectomy. Four of these 7 patients have asymptomatic gallstones detected incidentally during ultraso-

Table 1. Characteristics of Patients With Known Gallstones and All Transplant Recipients Analyzed Using the Student *t* Test

Characteristic	No. of Patients	Mean (SD)	Median	Range	*t*	*P*
Age, y						
Patients with known gallstones	36	49.97 (8.3)	50	29-66	3.25	.001
All patients	645	43.1 (12.5)	46	6-65		
Body mass index*						
Patients with known gallstones	36	24.5 (3.27)	24.3	18.1-34.6	3.13	.001
All patients	585	22.6 (3.55)	22.66	12.23-33.06		
Maximum transplant bilirubin level, µmol/L (mg/dL)						
Patients with known gallstones	36	55.1 (3.2) (36.6)	46 (2.7)	20-200 (1.2-11.7)	1.43	.08
All patients	645	66.9 (3.9) (48.7)	56 (3.3)	16-329 (0.9-19.2)		
Cyclosporine dosage, mg/kg						
1 month						
Patients with known gallstones	35	7.6 (4.19)	7.5	0.71-17.9	1.18	.12
All patients	539	6.77 (4.02)	6.4	0.43-32.11		
3 months						
Patients with known gallstones	34	5.53 (2.87)	5.6	0.9-12.3	0.67	.25
All patients	507	5.13 (3.37)	5.0	0.46-40		
6 months						
Patients with known gallstones	34	4.77 (2.02)	4.5	1.1-9.3	0.39	.35
All patients	476	4.56 (3.07)	4.5	0.17-36.8		
12 months						
Patients with known gallstones	34	4.55 (2.61)	4.2	0.6-13	0.86	.2
All patients	455	4.14 (2.69)	4.1	0.26-29.7		

**Obtained by dividing the weight (in kilograms) by the height (in meters) squared.*

Table 2. Characteristics of Patients With Known Gallstones and All Transplant Recipients Analyzed Using χ^2 Test

Variable	Patients With Known Gallstones	All Patients	χ^2	*P*
Sex				
Male	22	462	3.95	.05
Female	14	147		
Diabetes mellitus				
Yes	4	59	0.08	.78
No	32	550		
Cholestyramine administration				
Yes	6	65	1.83	.18
No	30	580		

nographic or computed tomographic scanning for unrelated conditions. These patients have had gallstones diagnosed for 67 months, 61 months, 16 months, and 15 months, respectively, without having symptoms related to the gallstones, and they have not been recommended for cholecystectomy. Two of these 7 patients are on the waiting list for cholecystectomy. Both have gallstones. One patient has had biliary colic intermittently during a 5-year period; the other patient has a 6-month history of biliary colic. The final patient with known gallstones who did not have cholecystectomy was a 54-year-old male heart and lung transplant recipient. He was admitted to the hospital with severe acute pancreatitis, acute renal failure, and respiratory failure 21 months after transplantation. Ultrasonography showed gallstones. The patient was considered too ill for laparotomy and cholecystectomy and he died 57 days after admission of pancreatitis and multiorgan failure.

The remaining 29 patients had cholecystectomy for symptomatic cholelithiasis and are analyzed as a group. Details on these patients are given in **Table 3**. Twenty-two were heart transplant recipients, 5 were heart and lung transplant recipients, and 2 were single lung transplant recipients. The proportions of each transplant type in the cholecystectomy sample group were not significantly different from the proportions of transplantations in the total transplant recipient group (χ^2 test, P=.26). The median interval from transplantation to cholecystectomy was 30 months. For the 23 patients for whom reliable information is available, the median symptomatic period for gallstone disease was 5 months. Symptoms included right hypochondrial pain in all 29 patients and nausea with or without vomiting in 14 patients. Sixteen patients had right upper quadrant tenderness on physical examination; 2 patients had fever. The median preoperative white blood cell count was within the normal range. Most liver function test results were abnormal, and only 3 patients had all the preoperative liver function test results for levels of bilirubin, alkaline phosphatase, alanine transaminase, and γ-glutamyltransferarse within the normal range. Four patients had an abnormally low serum albumin level.

Sixteen cholecystectomies were classified as elective, 7 as urgent, and 6 as semi-urgent. The median American Society of Anesthesiologists grade of anesthetic risk was 3 for the 20 patients for whom this information is available (Table 3). The minilaparotomy method of cholecystectomy was used for 16 patients, 11 patients had laparoscopic cholecystectomy, and 2 patients who were operated on in the prelaparoscopic era had open cholecystectomy. Twenty-two patients had operative cholangiography. Five of the 7 patients who did not have operative cholangiography had preoperative endoscopic retrograde cholangiopancreatography (ERCP), with removal of a stone from the common bile

Table 3. Characteristics of Patients Who Had Cholecystectomy for Symptomatic Gallstone Disease as Primary Operation*

	No. of Patients	Mean	Median	Range	Normal Range
Age, y	29	50.4	50	29-66	. . .
Interval from transplant to cholecystectomy, mo	29	31.8	30	2-103	. . .
Duration of biliary symptoms, mo	23	9.59	5	0-60	. . .
ASA grade†	20	2.6	3	2-4	1-4
Maximum preoperative test results					
White blood cell count, $\times 10^9$/L	29	8.66	8	5.5-21	4.0-11.0
Bilirubin level, μmol/L (mg/dL)	29	31.8 (1.8)	30 (1.8)	2-103 (0.1-6.0)	<18 (<1.0)
Alkaline phosphatase level, U/L	29	135.1	81	42-451	30-100
ALT level, U/L	29	42.17	22	6-163	<30
GGT level, U/L	29	194.76	59	11-1483	<35
Albumin level, g/L	29	40.43	41	29-46	36-47
Postoperative stay, d‡	28	3.79	3	1-25	. . .
Follow-up, mo‡	28	32.3	33	2-84	. . .

*ALT indicates alanine transaminase; GGT, γ-glutamyltransferase; and ellipses, not applicable.
†American Society of Anesthesiologists grade of anesthetic risk.
‡Excludes 1 patient who died on the second postoperative day.

duct in 2 of those patients. Three patients had abnormal operative cholangiogram results showing common bile duct calculi. These 3 patients had postcholecystectomy ERCP for common bile duct clearance. Only 1 patient, who had conventional open cholecystectomy in 1988, had removal of common bile duct stones by open choledochotomy rather than by ERCP. Only 2 patients had no imaging of the common bile duct and hepatic ducts.

Duration of postoperative stay ranged from 1 to 25 days, with a median of 3 days (Table 3). Four patients (13.8%) suffered postoperative complications. Two patients had postoperative right basal pulmonary atelectasis after urgent laparoscopic cholecystectomy and a third patient was mildly confused postoperatively. The fourth patient, a 47-year-old heart transplant recipient who had semi-urgent open cholecystectomy for acute cholecystitis with choledochotomy for common bile duct stone removal, had biliary peritonitis after the T tube was removed on the 14th postoperative day. This patient required a second laparotomy for closure of the common bile duct defect, and discharge from hospital was delayed until 25 days after cholecystectomy. There was 1 operative death—a 38-year-old man who had heart and lung transplantation for congenital heart disease. This patient was admitted to the hospital 1 week after discharge from the initial transplant admission and 2 weeks before cholecystectomy with a staphylococcal sternal wound infection that required rewiring of the sternum and a persistent right pleural effusion that required right lung decortication. *Pseudomonas* pneumonia with lung abscesses developed, and he needed urgent intubation on the day of cholecystectomy for respiratory failure. Gastroscopy examination to investigate epigastric pain showed bleeding gastric stress ulcers, but ultrasonographic testing results demonstrated multiple small gallstones and an urgent laparotomy for cholecystectomy was performed. Two days after cholecystectomy the patient died of respiratory failure caused by bronchopneumonia with abscess formation and pleural effusions. Histopathological examination of the gallbladder showed chronic cholecystitis.

Follow-up information is available for a median of 33 months (Table 3). Five additional patients have died of diseases unrelated to the biliary system between 15 and 33 months after cholecystectomy. Four patients, all of whom had intraoperative cholangiograms showing normal extrahepatic bile ducts, have had further biliary problems. Two of these patients have required ERCP for removal of common bile duct calculi. One patient had ERCP at 15 months after cholecystectomy with no further problems in the 9 months since then. The other patient has needed 3 ERCP procedures during a 10-month period for recurrent bile duct stones, but is currently well. A third patient had right upper quadrant pain 41 months after cholecystectomy. This patient has intrahepatic stones seen on ultrasonographic examination but refuses further treatment or investigation. Another patient experienced persistent right-sided hypochondrial pain after cholecystectomy and the condition has been diagnosed as biliary dyskinesia. This patient has had no pain for 12 months after an endoscopic sphincterotomy, performed 2 months after cholecystectomy. The remaining patients have had no symptoms suggestive of biliary disease after cholecystectomy.

COMMENT

This study found that only a minority of cardiothoracic organ transplant recipients have symptomatic gallstones, and that cholecystectomy by either minilaparotomy or laparoscopic methods, with preoperative or postoperative ERCP for common bile duct stones, is a safe and effective treatment for gallstone disease in most cases. Approximately 5% of 645 transplant recipients had symptomatic gallstone disease in this study, and 27 transplant recipients had minilaparotomy cholecystectomy or laparoscopic cholecystectomy, with minimal morbidity, no mortality, and a median postoperative stay of approximately 3 days.

Several factors have been suggested as contributing to the increased incidence of gallstones in cardiothoracic transplant recipients. These include corticosteroid-associated obesity, diabetes mellitus (which may also be due to corticosteroid use), and the use of the antirejection drug cyclosporine, which causes cholestasis.[7-9] This study compared the prevalence of these and other factors in the group of

patients with known gallstones and in the transplant recipient group as a whole. The validity of this comparison is weakened by the fact that routine ultrasonographic screening for gallstones is not conducted at this hospital, and it is thus likely that some patients with unrecognized gallstones are excluded from the gallstone group. Patients with known gallstones had a significantly higher body mass index, were significantly older, and a significantly higher proportion of them were women. They were no more likely to be diabetic, and had not received significantly more cyclosporine in the first 12 months after transplantation. Cyclosporine cholestasis is reflected mainly by an elevated serum bilirubin level,[9] but there was no difference in maximum bilirubin level during the transplantation admission between the 2 groups. The cholelithogenic drug cholestyramine has not been used at this hospital for the treatment of hypercholesterolemia in transplant recipients for several years, but 10% of the total number of transplant recipients nevertheless received this drug. There was no significant difference in the proportion of patients in each group who were given cholestyramine.

The minilaparotomy method of cholecystectomy was used for 16 of the 29 patients analyzed in this study. Minilaparotomy cholecystectomy involves removal of the gallbladder through a small transverse incision (typically 6 cm or less) in the right hypochondrial region. Minilaparotomy cholecystectomy has been shown to be comparable to laparoscopic cholecystectomy in most respects.[16-19] It is a particularly suitable method for use in cardiothoracic transplant recipients because, unlike laparoscopic surgery, it does not involve creation of a pneumoperitoneum and thus avoids the cardiac and pulmonary effects associated with a raised intra-abdominal pressure. These effects are dependent on the level of intra-abdominal pressure and are not reproducible in all studies, but include increased mean arterial pressure,[20,21] increased systemic[20] and calculated total peripheral resistance,[21] and decreased cardiac output[20] and cardiac index[21,22] owing to reduced venous return. Decreased stroke volume[22] may produce an increase in heart rate to maintain cardiac output.[23] This compensatory increase in heart rate may not be possible for denervated transplant recipients. Use of the highly soluble gas carbon dioxide for peritoneal insufflation produces carbon dioxide absorption,[24,25] and a significant increase in minute ventilation is required to prevent hypercarbia.[25] Patients with cardiopulmonary disease having laparoscopic cholecystectomy have been shown to have more severe hypercapnia and acidosis than patients with normal cardiopulmonary function.[26] Finally, the raised intra-abdominal pressure may decrease diaphragmatic excursion,[26] leading to decreased end-expiratory tidal volume, an increased physiological dead space, and ventilation-perfusion mismatch.[25,27] Despite these effects, several authors have emphasized that laparoscopic procedures can be safely performed in high-risk cardiac patients and transplant recipients if close intraoperative monitoring is provided.[4,20,22,28-30] In this study, both laparoscopic and minilaparotomy cholecystectomy were well tolerated, and mortality and major morbidity was limited to patients who had undergone open cholecystectomy. The same finding was reported by another group that specifically compared open and laparoscopic cholecystectomy in various transplant recipient groups, including heart transplant patients.[28] Either the minilaparotomy or laparoscopic methods of minimally invasive cholecystectomy are suitable for cardiothoracic transplant recipients, and are preferable to conventional open methods in most cases.

Most precholecystectomy results for the liver function tests of serum bilirubin, alkaline phosphatase, alanine transaminase, and γ-glutamyltransferase levels were abnormal, and only 3 patients had all liver function test results within the normal range. This suggests that most transplant recipients with gallstones undergoing cholecystectomy will require some contrast imaging of the common and hepatic bile ducts at or before operation. The later development of common or intrahepatic bile duct calculi in 3 patients who had normal bile ducts at the time of cholecystectomy further supports the concept of perioperative cholangiography, and suggests that this should be routinely performed to provide a baseline cholangiogram. Major morbidity or mortality are common complications of acute pancreatitis in transplant recipients,[4,31,32-38] so that, although the incidence of post-ERCP pancreatitis is low, imaging of the bile ducts may be better provided by routine operative cholangiography, with ERCP reserved for treatment of common or hepatic duct stones.

THE MANAGEMENT of asymptomatic gallstones in cardiothoracic transplant patients is controversial, with several authors advocating cholecystectomy for patients with asymptomatic gallstones.[3,4,6,13,14,31] Information supporting cholecystectomy for asymptomatic gallstones is of several types. First, the prevalence and incidence of gallstones in the transplant population seems high enough to warrant ultrasonographic screening of all patients if intervention is to be performed. Spes et al[1] screened 29 patients for gallstones with ultrasonography before and after transplantation. Two of 3 women but none of 26 men had gallstones before transplant surgery. After transplantation, 9 (35%) of the 26 males had gallstones within 43 months.[1] Another study found gallstones, sludge, cholesterol crystals, or cholesterol polyps in 27 (45%) of 60 patients, and 40% of transplant recipients had cholecystectomy in that study.[4] Second, the morbidity and mortality associated with urgent cholecystectomy in reported series of transplant recipients is considerably higher than the morbidity and mortality associated with elective operation. A study by Begos et al[13] in 1995 reviewed the results of their own and all previously published series, finding a mortality rate for urgent posttransplant cholecystectomy of 44% (8 of 18 cases), whereas there was no mortality for elective posttransplantation cholecystectomy (53 cases).[13] The worse results for urgent operations, presumably due to the rapid clinical deterioration of immunosuppressed transplant recipients with acute cholecystitis, support early elective cholecystectomy for gallstones before they become acutely symptomatic. Third, 2 studies have reported that many transplant recipients with asymptomatic gallstones will become symptomatic within a short time.[4,6] One study found that symptoms developed within 2±1.2 (SD) years in 7 (58%) of the 12 patients with asymptomatic gallstones diagnosed before transplantation,[4] while symptoms developed in 45% of the patients in another study.[6]

This study cannot reliably comment on the management of asymptomatic gallstones because routine ultrasonography is not practiced at this hospital and it is thus likely

that some or even most patients with asymptomatic gallstones remain undetected in this transplant population. However, 4 patients with asymptomatic gallstones in this study have remained asymptomatic for between 15 and 67 months, suggesting that some transplant recipients may be safely observed. Findings from another study,[2] in which most patients had pretransplant ultrasonographic screening, noted pretransplant asymptomatic cholelithiasis in 16 (16%) of 99 patients, and asymptomatic biliary sludge in 8 patients (8%). Only 1 of the 16 patients with asymptomatic cholelithiasis became "significantly" symptomatic after an average of 15 months after transplantation, and none of the patients with biliary sludge had symptoms after an average of 32 months.[2] The results for urgent cholecystectomy in the present series are better than the collected results presented by Begos et al,[13] suggesting that asymptomatic gallstones may be safely managed when they become symptomatic, even if symptoms develop acutely. In this series, 13 of the 29 patients who had cholecystectomy for symptomatic gallstones had urgent or semi-urgent operation. The only morbidity was right basal atelectasis in 2 patients. There was 1 death, in a heart and lung transplant recipient with an established chest infection who died of pneumonia 2 days after operation and for whom, in retrospect, cholecystectomy should not have been performed at that time. The 44% mortality rate for urgent posttransplant cholecystectomy found in collected series by Begos et al[13] may represent publication bias by authors reporting their adverse experiences. This possibility is supported by the few patients in those series—there were only 18 urgent cases in the 13 series or case reports reviewed. Indeed, the total number of posttransplant cholecystectomies in those 13 publications was only 74 cases.[13]

Support for routine cholecystectomy for transplant recipients with asymptomatic gallstones is provided by the history of 1 patient in the present study, however. This patient, who was not known to have gallstones and who did not have cholecystectomy, died of presumed acute gallstone pancreatitis. This patient's death might have been prevented by a policy of screening for gallstones with early removal of asymptomatic stones. The cost of such a policy would be considerable. Estimates of the total cost of uncomplicated laparoscopic cholecystectomy with operative cholangiography in Australia vary from $3745 (US $2921)[39] to $4646 (US $3858),[40] while the reported cost of this operation in the United States varies from $1589[41] to $5390[42] or more.[43] Accepting the finding of Peterseim et al[4] that 45% of cardiothoracic transplant patients develop gallstones,[4] 209 transplant recipients may have required cholecystectomy at this hospital during the past 12 years. The cost of nonlaparoscopic cholecystectomy in previous years is unknown, but using the lower estimate for laparoscopic cholecystectomy in Australia given above, the total cost of cholecystectomy for this hospital for 209 cholecystectomies would be US $610 489. This amount seems less significant, of course, when compared with the very large initial and ongoing costs associated with cardiothoracic organ transplantation itself.

The 3 patients in this series and 2 patients in another series[6] who have developed common bile duct or intrahepatic stones after cholecystectomy indicate that even removal of the gallbladder in all transplant recipients with gallstones will not fully protect against calculous biliary disease. These patients suggest the possibility that transplant patients are predisposed to stone formation even after cholecystectomy, perhaps because of the continuing presence of factors that contribute to the high incidence of gallbladder stones.

Cardiothoracic organ transplant recipients with symptomatic gallstones should have early cholecystectomy, preferably by either the minilaparotomy or laparoscopic methods, with routine operative cholangiography. Only 5% of 645 transplant recipients have had symptomatic gallstone disease in this series. The place of routine cholecystectomy for asymptomatic gallstones, which may develop in more than 40% of all transplant recipients according to other studies,[4] remains unclear. A trial in which transplant recipients with asymptomatic gallstones are randomized to either cholecystectomy or observation may help resolve this issue.

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1995 Update of the Working Group Reports on Chronic Renal Failure and Renovascular Hypertension
National High Blood Pressure Education Program Working Group

To update 2 National High Blood Pressure Education Program working group reports on hypertension and chronic renal failure and renovascular hypertension, a working group was appointed by the director of the National Heart, Lung, and Blood Institute. Literature was searched through MEDLINE and the National Heart, Lung, and Blood Institute information center library. Scientific evidence was given precedence over clinical anecdotal experience. The working group members produced initial draft documents that were circulated to additional experts on hypertension and renal disease. This reiterative process occurred for 18 draft documents. The final report was sent to the representatives of the 44 organizations on the Coordinating Committee for vote and unanimously approved September 1, 1995. The report recommended treatment of hypertension to the goal of 130/85 mm Hg with whatever therapy is necessary to prevent the development of hypertensive nephrosclerosis or the progression of established renal disease of diverse causes. It seems reasonable to recommend angiotensin-converting enzyme inhibitors as initial therapy for patients with diabetes and microalbuminuria or overt diabetic nephropathy with and without hypertension. Renovascular disease has emerged as a major cause of end-stage renal disease, especially in the elderly. Newer screening procedures for the noninvasive screening of renovascular disease include the captopril test, renal scintigraphy following captopril administration, duplex scanning, and magnetic resonance angiography. *Arch Intern Med. 1996;156:1938-1947*

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