Cholecystectomy in Sickle Cell Anemia Patients: Perioperative Outcome of 364 Cases From the National Preoperative Transfusion Study

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Cholecystectomy is the most common surgical procedure performed in sickle cell anemia (SCA) patients. We investigated the effects of transfusion and surgical method on perioperative outcome. A total of 364 patients underwent cholecystectomy: group 1 (randomized to aggressive transfusion) 110 patients; group 2 (randomized to conservative transfusion) 120 patients; group 3 (nonrandomized nontransfusion) 37 patients; and group 4 (nonrandomized transfusion) 97 patients. Patients were similar except group 3 patients were more likely to be female, over 20 years old, smokers, and more healthy by American Society of Anesthesiologists (ASA) physical status score. Total complication rate was 39%: sickle cell events 19%; intraoperative or recovery room events 11%; transfusion complications 10%; postoperative surgical events 4%; and death 1%. Group 3 patients had the highest incidence of sickle cell events (32%). Open cholecystectomies were performed in 58% and laparoscopic in 42%. Laparoscopic patients were younger and more healthy by ASA score. Laparoscopic patients had longer anesthesia time (3.2 *v* 2.9 hours), but shorter hospitalization time (6.4 days *v* 9.8). Complications were similar between these two groups. We conclude that SCA patients undergoing cholecystectomy have a high perioperative morbidity, and the incidence of sickle cell events may be higher in patients not preoperatively transfused. We recommend a conservative preoperative transfusion regimen, and we encourage the use of the laparoscopic technique for SCA patients undergoing elective cholecystectomy.

CHOLELITHIASIS IS VERY common in patients with sickle cell anemia (SCA), prevalence rates ranging from 30% to 70% depending on age and diagnostic criteria.[1-5] Cholecystectomy for both symptomatic and asymptomatic gallstones is commonly performed in patients with this disease, and it is the most frequently performed surgical procedure in this population.[6] However, debate continues concerning risks and optimal perioperative management for SCA patients undergoing cholecystectomy.

We have previously reported the results of the multiinstitutional, prospective, and randomized Preoperative Transfusion Study that investigated conservative versus aggressive transfusion in 604 surgical procedures in patients with SCA.[7] In this study, cholecystectomy comprised almost 40% of the procedures performed. The study included a registry of an additional 523 patients with SCA who underwent surgery at participating centers, but who were not randomized for preoperative transfusion therapy (ie, patients who were not transfused preoperatively or who were transfused without randomization). A total of 364 patients from both the randomized population and the nonrandomized registry underwent cholecystectomy, nearly all for symptomatic cholelithiasis. In this report, we compare the patient profile, perioperative management, risk factors, and outcome among the different preoperative transfusion groups. In addition, we compare the effect of open versus laparoscopic cholecystectomy on outcome.

MATERIALS AND METHODS

Patients were enrolled from 36 centers. Each institution had a principal investigator, nurse, and data coordinator, as well as an anesthesiologist and a surgeon in most cases. As previously described, a protocol was followed from patient registration through the 30-day postoperative follow-up period, and patient data were collected during this complete perioperative period. Institutions were randomly site-visited for verification of patient records.[7]

Patient population. Patients were eligible for randomization to a preoperative transfusion group if they had a diagnosis of hemoglobin SS or S-beta-0 and were undergoing elective surgery (defined as surgery occurring 24 hours or longer after registration). These patients were randomized to one of two transfusion groups: group 1, Aggressive Transfusion to obtain a preoperative hemoglobin of 10 g/dL (range, 9 to 11) and hemoglobin S percent of 30 or less; or group 2, conservative transfusion, to obtain a hemoglobin of 10 g/dL (range, 9 to 11), independent of hemoglobin S percent.

Patients were eligible for study registry, but not randomization, if they had been transfused within 3 months before surgery or if they or their physicians declined randomization. These patients were registered in one of two groups: group 3, nontransfusion; or group 4, nonrandomized transfusion. Seventy percent of patients in group 3 were not transfused due to the discretion of the principal investigator; 8% due to parent/patient refusal; and 22% for unstated reasons. Thirty-two percent of patients in group 4 were excluded from randomization due to recent blood transfusion; 27% due to parent/patient refusal; 21% due to discretion of the principal investigator; the remainder for unstated reasons. Approximately 53% of the patients in groups 3 and 4 were registered late (within 3 weeks of surgery).

From August 1988 through August 1993, 398 patients with SCA

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undergoing cholecystectomy at a participating institution were enrolled in the study after informed consent. Thirty-four patients were subsequently removed from enrollment due to cancellation of the procedure or ineligibility due to incorrect hemoglobinopathy diagnosis.

Perioperative management and data collection. Primary surgical procedure, incidental procedures, and surgical method were determined by the attending surgeon in consultation with the attending hematologist. The standardized treatment and transfusion protocols have been described previously.[7] Patients in the randomized groups were transfused so that their final preoperative hemoglobin was between 9 g/dL and 11 g/dL, but the decision to use exchange or simple transfusion was made by the local investigator. All patients received sickle-negative blood and, if there was a history of febrile transfusion reactions, leukocyte-depleted blood.[8]

The patients' medical history and information regarding perioperative transfusions, surgery, anesthetic management, and recovery period were recorded. Each patient's anesthetic risk (ie, American Society of Anesthesiologists, or ASA physical status) was determined,[9] and extensive perioperative laboratory information was obtained.[7] Complications occurring from study entry through a 30-day follow-up period were monitored and classified as minor, serious, or life-threatening. Most intraoperative and recovery room complications were graded as serious. Six additional serious or life-threatening complications were specifically defined: alloimmunization, vaso-occlusive pain crisis, acute chest syndrome (ACS), neurologic dysfunction, renal dysfunction, and fever with infection.[7] Vaso-occlusive crisis and ACS are considered to be unique to this population and were analyzed in detail as ''sickle cell events.''

Statistical analysis. Serious and life-threatening complication rates were compared across the four transfusion groups using the chi-square or Fisher exact tests for proportions. Confidence intervals were two-sided and a *P* value of .05 or less was considered significant. Patients undergoing laparoscopic cholecystectomy were compared with those undergoing open cholecystectomy using chi-square and Fisher exact tests. For comparison of means, the Student's *t*-test or an analysis of variance (ANOVA) was applied where appropriate.

To determine risk factors for complications, multivariate logistic regression models were developed for the presence or absence of any serious or life-threatening complication and of a sickle cell event. The models included age and any variable with significant univariate relationship ($P \leq .05$) to these outcome variables.

A multiple regression model was developed for the number of days of patient hospitalization. Independent variables included age, transfusion group, and risk factors with significant univariate relationship ($P \leq .05$) to the number of days of hospitalization.

RESULTS

Patient profile. A total of 364 patients underwent cholecystectomy: 110 in group 1, 120 in group 2, 37 in group 3, and 97 in group 4 (Table 1). Of the total population, 21% were less than 10 years of age and the youngest was 2.6 years. Ninety-eight percent of the patients had symptomatic cholelithiasis, although complete information about chronicity of symptoms was not available for all patients. One third of all patients had a history of significant pulmonary disease, defined as previous episodes of ACS, recurrent pneumonia, emphysema, or tuberculosis. An additional 4% had a history of asthma; 4% had baseline hypoxia (ie, PaO_2 less than 60 mm Hg or oxygen saturation less than 90% in room air); 11% had an abnormal baseline chest roentgenogram. Twenty-one percent had baseline elevation of serum glutamate pyruvate transaminase. The clinical and laboratory characteristics of patients in randomized groups 1 and 2 were similar to each other and to those in the nonrandomized transfused group 4. The patients in nontransfusion group 3 were significantly older ($P \leq .001$), and they tended to be female, healthier by ASA score, and smokers. For groups 3 and 4, there was no difference in all patient characteristics between those patients registered before and those registered after surgery.

Transfusion preparation. The preoperative hemoglobin and hemoglobin S levels were 10.5 g/dL) and 48%, respectively for the population at large, nearly one third of whom received an exchange transfusion in the perioperative period (Table 2). The preoperative hemoglobin values in groups 1 and 2 were similar, while their preoperative hemoglobin S percent differed, as expected by the study's transfusion protocol. Preoperative hemoglobin and S percent in group 4 were similar to that of group 1. The nontransfusion group 3 had the lowest preoperative hemoglobin and highest hemoglobin S percent. Six patients in this group received blood: two for operative blood loss, three for postoperative complications, and one for both.

Perioperative management. Preoperative, intraoperative, and postoperative management for all patient groups was generally uniform: 88% received preoperative hydration; 93% were monitored intraoperatively according to protocol; and 90% were provided with at least one intraoperative modality of body temperature conservation. General anesthesia with inhalation and intravenous agents was used in 91%, and combined epidural-general anesthesia was used in 8%. Postoperative analgesia was provided in all patients: intravenous narcotics in 92%, patient-controlled analgesia in 16%, and epidural analgesia in 10%. Postoperative oxygen therapy was provided in 96%, intravenous hydration in 100%, antibiotic therapy in 84%, and incentive spirometry in 42%. There were no differences among the four groups of patients in any of these aspects of perioperative care.

Complications. The overall complication rate was 39% percent (Table 3). A sickle cell event (ie, vaso-occlusive pain episode and/or ACS) occurred in 18% of patients and was more frequent in group 3 patients: 12% in group 1, 19% in group 2, 32% in group 3, and 18% in group 4 ($P = .041$). The rate of sickle cell events remained significantly higher in group 3, even when all retrospectively-registered patients were excluded from analysis. Intraoperative/recovery room events (eg, oxygen saturation <90%, temperature <35.5°C or >38.5°C, blood loss > than 10% of blood volume) occurred in 11%. Significant bleeding occurred in 22 patients (6%), 7 of whom required exploratory laparotomy following cholecystectomy for control of bleeding. Bleeding was not correlated with patient group, surgical technique (open *v* laparoscopic), or baseline elevation of the index liver function test. Neurological complications occurred only in group 4 patients ($P = .040$), many of whom were on chronic transfusion protocols for neurologic disease. Use of epidural anesthesia-analgesia in the intraoperative and/or postoperative periods had no correlation with postoperative complications.

Three deaths occurred in the study population, two in group 3 and one in group 4. A 13-year-old boy underwent open cholecystectomy without preoperative transfusion. His course was uncomplicated until 48 hours postoperatively when he developed ACS and respiratory failure, which progressed to death on the 10th postoperative day. This patient

Table 1. Clinical and Laboratory Characteristics of Cholecystectomy Patients

	Group 1 (Randomized Aggressive Tx) % (N = 110)	Group 2 (Randomized Conservative Tx) % (N = 120)	Group 3 (Nontransfusion) % (N = 37)	Group 4 (Nonrandomized Transfusion) % (N = 97)	Total % (N = 364)
Sex					
Male	57	56	38	52	53
Female	43	44	62	48	47
Age (yr)					
0-9	24	23	0	25	21
10-19	52	51	16	51	48
20+	25	26	84*	25	31
Mean age	16.2	16.5	28.0*	16.5	17.6
ASA physical status†					
ASA 2	50	49	62	44	49
ASA 3	48	50	38	55	49
ASA 4	2	1	0	1	1
Past medical history					
Pulmonary disease	35	30	38	33	33
Asthma	5	5	3	3	4
Smoking history	9	7	19	8	9
Cardiac disease	5	4	11	8	6
Renal disease	0	3	8	5	3
CNS disease	7	3	3	14	7
No. hospitalizations in past year					
None	27	20	24	18	22
1-4	64	68	57	67	65
5+	8	13	19	15	13
Average days hospitalized	7.1	8.4	8.9	9.7	8.4
Transfusion history					
No prior transfusions	22	25	22	18	22
<= 10 prior transfusions	54	53	57	56	54
> 10 prior transfusions	24	23	22	26	24
Alloimmunized	19	10	19	11	14
Previous transfusion reactions	5	4	5	8	6
Preoperative screening labs					
Preoperative hypoxia	3	6	4	2	4
Abnormal CXR	12	7	10	18	11
Abnormal SGPT (>60 U/L)	16	17	21	31	21
Creatinine > 1.5 mg/dL	4	5	3	2	4

Abbreviations: Tx, transfusion; CNS, central nervous system; CXR, chest x-ray; SGPT, serum glutamate pyruvate transaminase.

* $P \le .0001$.

† ASA physical status scores range from 1 to 5, from healthy to preterminal preoperative conditions.[9]

received full supportive care, although exchange transfusion was delayed due to difficulty in obtaining compatible blood. An 18-year-old boy underwent open cholecystectomy without transfusion during what appeared in retrospect to be an acute hepatic sequestration crisis. The postoperative course was complicated by hemorrhagic shock and coagulopathy. On the 10th postoperative day, the patient died after an attempted computed tomography (CT)-guided needle aspiration of an inflammatory mass around the gallbladder. A 40-year-old woman underwent open cholecystectomy following transfusions for a febrile illness thought to be acute cholecystitis, although her gallbladder showed no acute pathologic changes. She expired on the 20th postoperative day after a course complicated by ACS, pyelonephritis, *Haemophilus influenzae* pneumonia, coagulopathy with a large retroperitoneal hematoma, and possible transfusion reaction.

Open versus laparoscopic cholecystectomy. Fifty-eight percent of the cholecystectomies were open procedures and the remainder were laparoscopic[10] (Table 4). The development of the laparoscopic technique during the course of the study was reflected by a chronologic profile of the technique's application: 14% of the procedures during the first half of the study were laparoscopic, while 70% of those during the second half were laparoscopic. Five percent of the laparoscopic procedures were converted to open procedures and were analyzed as laparoscopic. The open and laparoscopic groups were similar in makeup except that patients in the laparoscopic group were older ($P = .027$) and healthier by ASA physical status score ($P = .011$), while those in the open procedure group were more likely to have baseline elevation of the index liver function test ($P = .0002$). Fourteen of the patients in the laparoscopic group were less than 10 years of age, and the youngest was 3.5 years.

Patients in the open and laparoscopic groups had similar preoperative hemoglobin levels (10.6 and 10.4 g/dL, respectively) (Table 5); hemoglobin S percent was 45% and 52%,

Table 2. Preoperative Hgb, S%, and Perioperative Transfusion Data

	Group 1 (Randomized Aggressive Tx) (N = 110)	Group 2 (Randomized Conservative Tx) (N = 120)	Group 3 (Nontransfusion) (N = 37)	Group 4 (Nonrandomized Transfusion) (N = 97)	Total (N = 364)
Mean preoperative Hb g/dL	10.9 (1.2*)	10.6 (1.2*)	8.6 (1.5*)†	10.7 (1.3*)	10.5 (1.4*)
Mean preoperative S%	34% (16*)	61% (15*)	88% (8*)†	38% (19*)	48% (23*)
% Transfused	100%	98%	16%†	97%	91%
% Exchanged	64%	7%	3%†	33%	31%
Mean No. units transfused	5.4 (2.7*)	2.7 (1.8*)	0.5 (1.4*)†	4.3 (3.4*)	3.7 (3.0*)

* Standard deviation.
† $P \leq .0001$.

respectively ($P \leq .01$). Administration of preoperative hydration, as well as the use of intraoperative monitoring and temperature control modalities occurred with similar frequency in the two groups. Combined epidural-general anesthesia was used in 13% of the open procedure patients and in only 1% of laparoscopic procedures ($P \leq .0001$). Postoperative administration of supplemental oxygen therapy and intravenous fluids also occurred with similar frequency in the two groups. However, open cholecystectomy patients were more likely than laparoscopic cholecystectomy patients to receive postoperatively epidural analgesia (17% *v* 1% [$P \leq .0001$]), parenteral antibiotics (89% *v* 76% [$P = .002$]), and incentive spirometry (50% *v* 31% [$P = .0003$]).

Open cholecystectomy patients were more likely than laparoscopic patients to have an intraoperative cholangiogram, to have common bile duct stones, and to undergo incidental procedures with cholecystectomy (Table 5). The most common of these incidental procedures were appendectomy (50 patients), liver biopsy (24 patients), and umbilical herniorrhaphy (13 patients). The two surgical groups had a similar frequency of extended procedures, ie, intended cholecystectomy, which was converted to choledochoduodenostomy, choledochojejunostomy, or hepatojejunostomy.

Total anesthesia time was shorter for open cholecystectomy than for laparoscopic (2.9 *v* 3.2 hours [$P = .007$]) (Table 5). This similarity persisted when those patients in each group who underwent incidental or extended procedures were excluded. Analysis of individual institutions that performed 10 or more laparoscopic cholecystectomies showed no chronologic decrease in anesthesia time, and the mean anesthesia time for all laparoscopic patients was 3.0 hours in the first half of the study and 3.3 hours in the second half. Hospitalization time in the open group was longer than in the laparoscopic group (9.8 *v* 6.4 days [$P = .0001$]). Total complication rate and the rate of all specific complications were similar in open and laparoscopic patients (Table 6).

Predictors of complication. To identify predictors of serious or life-threatening complications, 18 possible risk factors were abstracted from patient data (Table 7). In univariate analysis, older patients, patients with an extensive transfusion history, and those undergoing incidental procedures were more likely to have serious complications. In the multi-

Table 3. Perioperative Complications in Cholecystectomy Patients

After Start of Transfusion Regimen	Group 1 (Randomized Aggressive Tx) % (N = 110)	Group 2 (Randomized Conservative Tx) % (N = 120)	Group 3 (Nontransfusion) % (N = 37)	Group 4 (Nonrandomized transfusion) % (N = 97)	Total % (N = 364)
Intraoperative/recovery room	10	13	11	11	11
Acute chest	9	11	19	7	10
Pain	3	9	19	10	9
Fever	7	4	5	12	7
Surgical postoperative	4	4	5	4	4
Miscellaneous postoperative	1	3	5	6	3
Renal	0	1	3	1	1
Neuro	0	0	0	3†	1
Death	0	0	5	1	1
Any grade 2-3 event	27	34	43	38	34
Transfusion-related complications:					
New antibody	13	4	0‡	6	6
Transfusion reaction	9	4	3	4	6
Any transfusion-related	15	8	3	9	10
Total complications	36	39	43	41	39

* $P = .016$.
† $P = .040$.
‡ $P = .018$.

Table 4. Clinical and Laboratory Characteristics of Cholecystectomy Patients

	Open *v* Laparoscopic Cholecystectomy		
	Open Cholecystectomy % (N = 211)	Laparoscopic Cholecystectomy % (N = 153)	Total % (N = 364)
Sex			
Male	53	54	53
Female	47	46	47
Age (yr)			
0-9	25	17	21
10-19	47	48	48
20+	28	35	31
Mean	16.7	18.8*	17.6
ASA physical status			
ASA 2	44	58†	49
ASA 3	55	42	49
ASA 4	2	0	1
Past medical history			
Pulmonary disease	34	31	33
Asthma	4	5	4
Smoking history	7	11	9
Cardiac disease	8	5	6
Renal disease	3	3	3
CNS disease	7	8	7
No. hospitalizations in past year			
None	21	23	22
1-4	66	65	65
5+	13	12	13
Average days hospitalized	9.8	6.4	8.4
Transfusion history			
No prior transfusions	22	22	22
<= 10 prior transfusions	54	55	54
> 10 prior transfusions	24	24	24
Alloimmunized	15	12	14
Previous transfusion reactions	6	5	6
Preoperative screening labs			
Preoperative hypoxia	3	5	3
Abnormal CXR	11	12	11
Abnormal SGPT (>60 U/L)	27	12‡	21
Creatinine > 1.5 mg/dL	4	3	4

* $P = .027$.
† $P = .011$.
‡ $P = .002$.

variate logistic regression including these significant risk factors, only patient age and the presence of incidental procedures were independent predictors of any serious complication (Table 7). In the univariate analysis of 18 possible predictors of sickle cell events, absence of preoperative transfusion and a history of frequent hospitalization were significant risk factors. In the multivariate logistic regression including these two risk factors and patient age, absence of preoperative transfusion and frequent hospitalization remained as independent predictors of sickle cell events (Table 7).

Predictors of length of hospitalization. The average length of hospitalization was 8.4 days. In a univariate analysis of possible predictors of length of hospital stay, higher ASA physical status, positive transfusion history, baseline chest roentgenogram abnormality, open surgical technique, and presence of incidental procedures were factors that were significantly correlated with increased length of hospitalization. In the multivariate regression model including patient age and these risk factors, only higher ASA status, chest roentgenogram abnormality, and open surgical technique remained as significant independent predictors of increased length of hospitalization (Table 8).

DISCUSSION

Cholecystectomy is the most common surgical procedure performed in patients with sickle cell anemia.[6] This report of 364 patients with SCA and symptomatic cholelithiasis undergoing cholecystectomy constitutes the largest collection of this particular surgical population, and it provides

Table 5. Perioperative Profile: Open Versus Laparoscopic Cholecystectomy

	Open Cholecystectomy (N = 211)	Laparoscopic Cholecystectomy (N = 153)	Total (N = 364)
Transfusion			
Preoperative transfusion (%)	91	89	90
Preoperative Hgb g/dL	10.6 (1.5*)	10.4 (1.3*)	10.5 (1.4*)
Preoperative S%	45 (22*)	52 (22*)†	48 (23*)
Mean no. units transfused	3.8 (3.0*)	3.6 (2.9*)	3.7 (3.0*)
Procedures (%)			
Intraoperative cholangiogram	69	58‡	64
Common bile duct stones	14	6§	10
Incidental procedures	33	16‖	26
Extended procedures	1	1	1
Anesthesia time (h)	2.9 (1.0*)	3.2 (1.1*)¶	3.0 (1.1*)
Hospitalization time (d)	9.8 (6.5*)	6.4 (5.3*)#	8.4 (6.3*)

* Standard deviation.
† $P = .009$.
‡ $P = .028$.
§ $P = .015$.
‖ $P = .0002$.
¶ $P = .007$.
\# $P = .0001$.

important information concerning the perioperative outcome of these patients. We demonstrate that the rate of complication is high in these patients even with high-quality perioperative care, and that the rate of specific sickle cell events in patients who did not receive preoperative transfusion is increased compared with those who did. In addition, we demonstrate that laparoscopic technique decreases hospitalization time in this population without increasing complications.

The morbidity in our patients is higher than that of previous reports describing individual institutions with sickle cell patients undergoing open[11-17] and laparoscopic[18] cholecystectomy for both symptomatic and asymptomatic disease. These reports contained small numbers of patients (9 to 42) managed with different transfusion regimens, and these reports did not uniformly assess patient risk factors, or include transfusion-related complications. However, Griffin et al[19] did report a postoperative complication rate of 50% in a subset of their sickle cell patient population who underwent thoracotomy or laparotomy without preoperative transfusion. The mortality rate in our population is similar to that of previous reports (<5%).

Table 6. Perioperative Complications: Open Versus Laparoscopic Cholecystectomy

	Open Cholecystectomy % (N = 211)	Laparoscopic Cholecystectomy % (N = 153)	Total % (N = 364)
Intraoperative/recovery room	11	12	11
Acute chest	10	10	10
Pain	9	8	9
Fever	7	8	7
Surgical postop	3	5	4
Miscellaneous postop	2	5	3
Death	2	0	1
Renal	1	0	1
Neuro	<1	1	1
Death	2	0	1
Any grade 2-3 event	35	33	34
Transfusion-related complications			
New antibody	7	7	7
Transfusion reaction	6	5	6
Any transfusion-related	10	9	10
Total complications	40	38	39

The occurrence of any serious complication in the perioperative period was correlated with increased patient age and the presence of incidental surgical procedures. SCA patients beyond the second decade of life would be expected to have relatively high morbidity and mortality[20] even in the absence of surgery. However, it is not clear why incidental surgical procedures should affect outcome. These surgical procedures may affect morbidity by increasing anesthesia time, although anesthesia time itself was not an independent predictor of complications. Alternatively, the particular procedures performed in our patients as incidental procedures may be associated themselves with higher risk, although these procedures are, in fact, included in surgical risk categories that are equal to or less than that of cholecystectomy.[7]

The occurrence of specific sickle cell events (vaso-occlusive pain episodes and ACS) correlated with the number of previous hospitalizations and the absence of preoperative transfusion. The number of previous hospitalizations presumably reflects severity of clinical disease. The higher incidence of these events in patients who were not transfused preoperatively (group 3) compared with those who were transfused (groups 1, 2, and 4) suggests that there may be a role for preoperative transfusion in preventing sickle cell events in patients undergoing cholecystectomy.[13,19,21] How-

Table 7. Clinical and Laboratory Values as Risk Factors for Postoperative Complications

	Any Grade 2-3 (N = 124) %†	Odds Ratio* (95% CI)	ACS OR Pain (N = 65) %‡	Odds Ratio* (95% CI)
Sex				
Female	32		20	
Male	36		16	
Age (yr)				
<10	27	1.0	17	
10-19	33	1.39 (.75 to 2.56)	17	
20+	41	2.01 (1.05 to 3.86)	20	
History of CNS disease				
No	34		18	
Yes	37		19	
History of pulmonary disease				
No	32		16	
Yes	39		21	
History of renal or cardiac disease				
No	33		18	
Yes	47		19	
Previous hospitalizations				
None	24		13	1.0
1-4	35		16	1.33 (.63 to 2.86)
5+	40		31	3.02 (1.19 to 7.65)
ASA score				
2	32		17	
3-4	36		19	
Previous transfusions				
None	27		15	
1-10	34		16	
>10	42		26	
History of alloimmunization				
No	34		17	
Yes	35		22	
Arm				
Transfused (group 1, 2, 4)	33		16	1.0
Nontransfused (group 3)	43		32	2.79 (1.16 to 6.69)
Preoperative hemoglobin				
<9.0 g/dL	29		17	
>= 9.0 g/dL	35		18	
Preoperative hemoglobin S%				
<= 30%	28		13	
31-50%	35		15	
51-70%	31		17	
71-99%	43		27	
Preoperative chest x-ray				
Abnormal	39		26	
Normal	33		17	
Preop oxygen saturation < 90%				
No	34		17	
Yes	22		22	
Open procedure				
No	34		18	
Yes	34		18	
Incidental procedures				
No	30	1.0	17	
Yes	46	2.0 (1.22 to 3.29)	21	
Duration of anesthesia <= 2 h	43		21	
Duration of anesthesia > 2 h	32		17	
Epidural narcotics				
No	33		18	
Yes	41		19	

* Odds ratios with 95% confidence intervals were calculated for statistically significant independent predictors in the multivariate logistic analysis.
† Percentage of patients with a particular clinical attribute that developed any grade 2-3 complication.
‡ Percentage of patients with a particular clinical attribute who developed ACS or pain.

Table 8. Average Hospital Stay

	Mean ± SD	*P* Value*
ASA		
2	7.37 ± 5.23	.024
3-4	9.38 ± 7.02	
CXR		
Abnormal	10.87 ± 9.22	.046
Normal	8.10 ± 5.85	
Unknown	8.29 ± 6.04	
Open procedure	6.10 ± 4.93	.0004
Laparoscopic	9.81 ± 6.56	

* Significant independent predictors of duration of hospitalization in multiple regression model.

ever, because the number of patients undergoing cholecystectomy without preoperative transfusion was small, and because these patients were not randomly assigned to nontransfusion, our findings may not be generalizable.

While there is clinical and laboratory evidence to support the beneficial effects of dilution of sickle cells on outcome,[22-25] it is not certain if there is a threshold for such effects or if the effects are proportionate to the percentage of hemoglobin S. In vitro studies indicate that the interrelationship between total hemoglobin concentration and percent of hemoglobin S with blood viscosity and flow is complex and not strictly linear.[21,26-28] In this study, vaso-occlusive pain episodes were highest in the nontransfusion group (mean preoperative hemoglobin S 88%) and lowest in the randomized aggressive transfusion group (hemoglobin S 34%), a finding that may suggest there is a threshold percentage of hemoglobin S at which vaso-occlusive events are more likely to occur.

The subgroup of 153 patients undergoing laparoscopic cholecystectomy offers comparisons with previous reports of this procedure in general pediatric and adult populations.[29-36] The conversion rate from laparoscopic to open cholecystectomy in the general population (2% to 12%) [29,30,32,34] is similar to that of our patients (5%), while the complication rate for the general population undergoing laparoscopic cholecystectomy (4% to 5%) is considerably lower than in our population. Surgical time reported in the general population for the laparoscopic procedure (1 to 2 hours)[29-32] is shorter than that reported here (mean, 3.2 hours), although our time reflects total anesthesia time, not surgical time alone, and includes time for incidental procedures in 16% of cases. Hospitalization time for the general population is also shorter (1 to 2 days)[29,31,32] than for our population (mean, 6.4 days). All of these differences would seem to be attributable largely to the underlying disease of our patients and the complex perioperative care required by them.

Surprisingly, anesthesia time was shorter in the open cholecystectomy group than in the laparoscopic group, despite a larger proportion of the cases in the open group having simultaneous incidental procedures (33% *v* 16%). Operative time for laparoscopic procedures has been reported to be shorter than for open procedures in the general population.[29,34] The relatively long time for laparoscopic procedures in this study may reflect an institutional ''learning curve'' since the procedure was introduced during the course of the study, although we were unable to demonstrate this at individual participating institutions.

Perioperative outcome was similar for the open and laparoscopic cholecystectomy groups despite a higher average ASA physical status score and more frequent baseline liver dysfunction in patients in the open group. It is possible that patients in the open cholecystectomy group benefitted from more frequent use of such postoperative interventions as intravenous antibiotics, supplemental oxygen, and incentive spirometry.[37] The finding that morbidity was the same in the open and laparoscopic groups in our sickle cell population (unlike what is reported for the general population[29,34]) may well reflect the importance of the underlying disease, rather than the procedure, in determining perioperative outcome in our population.

Hospitalization time was longer for the open cholecystectomy group than the laparoscopic group (mean, 9.8 days *v* 6.4 days), and surgical technique was found to be an independent predictor of length of hospitalization. Hospitalization time was also directly correlated with patient ASA physical status score and baseline chest roentgenogram abnormality, factors which together may reflect medical conditions that would be expected to affect length of hospital stay. That laparoscopic cholecystectomy is associated with shortened hospitalization without increased morbidity is an important consideration in the current setting of health care priorities.

In conclusion, we have found in 364 patients with SCA undergoing cholecystectomy that total perioperative morbidity is 39%. While total morbidity is not affected by preoperative transfusion, the incidence of specific sickle cell events is higher in those patients who were not transfused preoperatively than in those who were. Laparoscopic cholecystectomy was accompanied by shorter hospitalization time (6.4 days) than was open cholecystectomy (9.8 days), although perioperative outcome was similar between the two groups. Therefore, based on findings in this and our previous report, we recommend conservative preoperative transfusion and use of the laparoscopic technique, where available, for patients with SCA undergoing cholecystectomy.

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APPENDIX

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