Surgery and Anesthesia in Sickle Cell Disease


From 1978 to 1988, The Cooperative Study of Sickle Cell Disease observed 3,765 patients with a mean follow-up of 5.3 ± 2.0 years. One thousand seventy-nine surgical procedures were conducted on 717 patients (77% sickle cell anemia [SS], 14% sickle hemoglobin C disease [SC], 5.7% Sβ⁰ thalassemia, 3% Sβ⁺ thalassemia). Sixty-nine percent had a single procedure, 21% had two procedures, and the remaining 11% had more than two procedures during the study follow-up. The most frequent procedure was abdominal surgery for cholecystectomy or splenectomy (24% of all surgical procedures, N = 258). Of these, 93% received blood transfusion, and there was no association between preoperative hemoglobin A level and complication rates (except reduction in pain crisis). Overall mortality within 30 days of a surgical procedure was 1.1% (12 deaths after 1,079 surgical procedures). Three deaths were considered to be related to the surgical procedure and/or anesthesia (0.3%). No deaths were reported in patients younger than 14 years of age.

Patients with sickle cell disease (SCD), which includes sickle cell anemia (SS), sickle hemoglobin C disease (SC), and the sickle β thalassemias) who undergo surgery are generally considered to be at greater risk for perioperative complications than otherwise healthy patients without this hematologic disorder. Favorable outcomes have been reported without transfusion, but perioperative transfusion is commonly used to prepare SCD patients for surgery and to treat complications of sickle cell disease. Although the optimal level of sickle hemoglobin (Hb) to be achieved is unknown, most sickle cell centers adhere to some form of transfusion protocol for SCD patients undergoing surgery.

The Cooperative Study of Sickle Cell Disease (CSSCD) was a natural history study that observed 3,765 patients from 1978 to 1988. This report analyzes the course and outcome of the 1,079 surgical procedures performed on 717 patients during this time period.

Materials and Methods

Patients

The goals, objectives, design, and enrollment procedures of the Cooperative Study of Sickle Cell Disease have been described elsewhere. From October 1978 to October 1988, 3,765 patients from 23 clinical centers across the continental United States participated in the CSSCD. The median length of patient follow-up was 6.0 years. Of the total study cohort, 67.5% of the patients had SS, 22.4% had the sickle β thalassemia (Sβ⁰ thal), and 5.1% had sickle β⁺ thalassemia (Sβ⁺ thal). The Hb phenotype was established by the Centers for Disease Control using standard laboratory methods.

Data Collection

A standardized CSSCD data collection form was completed each time a patient underwent a surgical procedure. Because of limitations in data collection procedures, only one surgical procedure was recorded per operation. Medical history, laboratory data, and perioperative course were recorded on this form. Separate forms were completed documenting blood transfusions and acute and chronic clinical events. Transfusion data for the 30-day period before surgery and acute event data for the 7-day period after surgery were used in this report. All deaths within 30 days after a surgical procedure are summarized in this report. Deaths occurring within 7 days of surgery were defined as postoperative complications.

Classification of Surgeries, Anesthesia, Transfusion, and Complications

Surgicale were defined using the International Classification of Diseases (9th revision) diagnosis codes for procedures. For the purposes of analysis, surgical procedures were categorized into three groups by level of risk: low, moderate, and high. Low-risk procedures are those of the eyes, skin, nose, ears, and distal extremities as well as those pertaining to the dental, perineal, and inguinal areas (eg, inguinal hernia repair, myringotomy, and dilatation and curettage). Moderate-risk procedures are those of the throat, neck, spine, proximal extremities, genitourinary system, and intra-abdominal areas, such as tonsillectomy, Cesarean section, splenectomy, cholecystectomy, and hip replacement. High-risk procedures are those pertaining to the intracranial, cardiovascular, and intrathoracic systems (eg, craniotomy and heart valve replacement).
In addition to overall analyses stratified by risk level, six specific classes of the most common surgical procedures were analyzed: (1) cholecystectomy or splenectomy (N = 222 and 36, respectively; 23.9% of all surgical procedures); (2) dilation and curettage (N = 97; 9.0%); (3) Cesarean section or hysterectomy (N = 87; 8.1%); (4) tonsillectomy and/or adenoidectomy (N = 46; 4.3%); (5) hip replacement, removal, or revision (N = 44; 4.1%); and (6) myringotomy (N = 30; 2.8%). The frequencies of the remaining surgical procedures (47.8%) are listed in the Appendix.

Anesthesia was classified as general, regional, and local. General anesthesia refers to that induced by the inhalation of gas and balanced intravenous methods. Regional anesthesia refers to spinal, epidural, and nerve block anesthesia. The type of anesthesia and its method of administration were not prescribed by the CSSCD protocol.

Patients were defined as preoperatively transfused if at least one transfusion was administered within 30 days before surgery. Postoperative complication rates for patients who were perioperatively (either preoperatively or intraoperatively) transfused were compared with those who were not transfused. Total Hb concentrations and Hb A percentages presented in this report were obtained after transfusion and before surgery. The CSSCD was a natural history study, thus no protocol was specified for perioperative management; all patients were treated according to institutional practices.

Postoperative complications were defined as complications that occurred within 7 days after surgery. These complications were categorized into three groups: (1) SCD-related, (2) non-SCD-related, and (3) other. SCD-related complications were defined as painful crisis, acute chest syndrome (ACS), and cerebrovascular accident (CVA). Non-SCD-related complications were defined as fever, infection (excluding ACS), bleeding, thrombosis, embolism, and death. Other postoperative complications included transfusion reactions and unspecified complications. Painful crisis was defined as pain in the extremities, back, abdomen, chest, or head for which no other explanation (eg, osteomyelitis or appendicitis) could be found. ACS was defined as the new appearance of an infiltrate on chest radiograph or abnormalities on a radioisotope lung scan in the presence of symptoms.

Statistical Methods
Because many patients underwent more than one surgical procedure, the surgery served as the unit of analysis; eg, percentages reported refer to the percentage of surgeries with a particular characteristic, rather than the percentage of patients. Complication rates are computed as the number of surgeries with a particular complication divided by the total number of surgeries. Descriptive statistics are presented as percentages and means ± 1 standard deviation. All hypothesis tests and confidence intervals are two-sided. A two-sided P value of .05 or less was considered to be a statistically significant result. Postoperative complication rates with and without perioperative transfusion were compared using logistic regression, with adjustment for phenotype, type of anesthesia, surgical risk level, and age. The logistic regression model provided robust standard error estimates for the model parameters that accounted for the correlation between different surgical procedures on the same patient.30 The association between postoperative complication rates and anemia was also examined using logistic regression. Where there were sufficient data, the association between postoperative complication rates (1) total Hb concentration and (2) Hb A percentage was examined using logistic regression. Mean total Hb concentrations of patients with and without postoperative complications were compared using the Student’s t-test.

RESULTS

General Characteristics
There were 717 patients who had one or more surgical procedures. Of these patients, 77.1% (N = 553) were SS, 14.2% (N = 102) were SC, 5.7% (N = 41) were Sβthal, and 2.9% (N = 21) were Sβthal. This group has proportionately more SS and fewer SC and Sβthal patients than the total CSSCD cohort (see Materials and Methods). Sixty-nine percent (N = 495) of the patients underwent one, 20.5% (N = 147) had two, 6.0% (N = 43) had three, and 4.5% (N = 32) had four or more surgical procedures during the follow-up period. Forty-eight percent (N = 520) of the 1,079 reported surgical procedures were classified as low-risk, 50% (N = 543) as moderate-risk, and 2% (N = 16) as high-risk procedures. Seventy-five percent (N = 806) were elective and 25% (N = 271) were emergent surgical procedures. The mean age at the time of surgery was 22.0 ± 11.6 years, with 17% being less than 10 years of age, 25% being 10 to 19 years of age, 52% being 20 to 39 years of age, and 6% being 40 years of age and older. Female patients underwent 61% (N = 660) of the surgical procedures and male patients underwent the remaining 39% (N = 419).

The reported sample includes surgical procedures of differing risk levels performed on patients of varying ages. The risk of postoperative complications significantly increased with age (estimated odds ratio, 1.3 times increased risk of postoperative complications per 10 years of age, P < .0001). Comparisons of postoperative complication rates were therefore adjusted for patient age as well as surgical risk level to correct for the potential confounding effects of these two factors.

Postoperative Deaths
There were 12 postoperative deaths (10 SS, 1 SC, and 1 Sβthal) within 30 days of a surgical procedure (Table 1). Notably, there were no deaths among patients under 14 years of age and only 2 in patients between 14 and 20 years of age. The mean age at death was 27.4 ± 10.4 years (range, 14 to 54 years). Eleven of these patients were transfused. There were 8 minor and 4 major intra-abdominal procedures. The deaths in the first 9 patients appear to be related to comorbid medical complications and SCD-related multiorgan failure. The deaths in the remaining 3 patients appear to be related to the surgical procedure: patient no. 10 from profound anemia secondary to delayed transfusion reaction; patient no. 11 from an intra-abdominal hemorrhage requiring 18 U of packed red blood cells; and patient no. 12 from rupture of the prosthetic mitral valve replaced 38 days earlier (the surgical procedure was a diagnostic right heart catheterization 1 day before death).

The overall 30-day postoperative mortality rate was 1.1% (12 deaths of 1,079 surgical procedures). The actual mortality rate of the 3 deaths related to the surgical procedure was only 0.3%.

A Profile of Most Frequently Performed Procedures
A description of six classes of surgical procedures most frequently performed during the course of the CSSCD is displayed in Table 2. There were few procedures performed on SC patients; thus, no formal statistical comparisons of the outcome of SS and SC patients were made. Analyses of the relationship between preoperative Hb A level and
postoperative complications were conducted only for two of the groups, ie, abdominal surgery (cholecystectomy and splenectomy) and orthopedic procedures of the hip. Only for these two groups were posttransfusion Hb A data available for at least 80% of the surgical procedures on SS patients.

Cholecystectomy and splenectomy. Patients undergoing open cholecystectomy had a mean age of 23.3 ± 1.1 years (range, 5 to 64 years). Patients undergoing splenectomy had a mean age of 7.8 ± 8.5 years (range, 9 months to 30 years). All procedures were performed under general anesthesia and the majority of patients were preoperatively transfused. The rate of SCD-related postoperative complications was similar for SS and SC patients (8% and 9%, respectively). Rates of non-SCD-related postoperative complications were 11% for SS and 23% for SC patients. The most frequent non-SCD-related complications were fever and infection (other than ACS).

There was no difference in the overall rates of postoperative complications in 203 transfused versus 13 untransfused SS patients (21.6% vs 33.3%, P = .229). When examined separately, SCD-related and non-SCD-related complication rates were again similar for transfused and untransfused SS patients.

### Table 1. Postoperative Deaths Occurring Within 30 Days of Surgery

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age/ Sex</th>
<th>Hb Diag.</th>
<th>Clinical Status at Surgery</th>
<th>Surgical Procedure</th>
<th>No. of Units of PRBC Transfused Within 30 d of Death</th>
<th>Preop Hb A %</th>
<th>Anesthesia</th>
<th>Surgery to Death (d)</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21/F</td>
<td>SS</td>
<td>Cirrhosis DIC, MOF, CRF</td>
<td>Bronchoscopy, mediastinoscopy</td>
<td>2</td>
<td>—</td>
<td>Local</td>
<td>18</td>
<td>ARDS</td>
</tr>
<tr>
<td>2</td>
<td>36/F</td>
<td>SS</td>
<td>Febrile</td>
<td>Tendon repair</td>
<td>2</td>
<td>—</td>
<td>Local</td>
<td>26</td>
<td>ARF</td>
</tr>
<tr>
<td>3</td>
<td>28/F</td>
<td>SS</td>
<td>MOF/sepsis, CRF, DIC peritonitis/pneumonia</td>
<td>Tenckhoff catheter</td>
<td>30</td>
<td>—</td>
<td>Local</td>
<td>9</td>
<td>Sepsis, DIC</td>
</tr>
<tr>
<td>4</td>
<td>27/F</td>
<td>SS</td>
<td>CRF/SP renal transplant clotted venous graft removal</td>
<td></td>
<td>4</td>
<td>95</td>
<td>Local</td>
<td>15</td>
<td>DOA</td>
</tr>
<tr>
<td>5</td>
<td>23/M</td>
<td>SS</td>
<td>CRF infected graft, dialysis</td>
<td>Graft removal</td>
<td></td>
<td>—</td>
<td>Local</td>
<td>29</td>
<td>Sepsis, M. TB</td>
</tr>
<tr>
<td>6</td>
<td>20/F</td>
<td>SS</td>
<td>CVA, comatose</td>
<td>Dental extraction</td>
<td>0</td>
<td>—</td>
<td>Local</td>
<td>12</td>
<td>DOA</td>
</tr>
<tr>
<td>7</td>
<td>54/F</td>
<td>SS</td>
<td>Acute abdomen, Bili 26, CHF</td>
<td>Exploratory cholecyst.</td>
<td>5</td>
<td>70</td>
<td>Inhale</td>
<td>4</td>
<td>ARF</td>
</tr>
<tr>
<td>8</td>
<td>17/F</td>
<td>SS</td>
<td>Sepsis, acidosis, MOF, DIC, ARF</td>
<td>Exploratory laparotomy</td>
<td>10</td>
<td>71</td>
<td>Inhale</td>
<td>2</td>
<td>DIC, Sepsis</td>
</tr>
<tr>
<td>9</td>
<td>26/F</td>
<td>SC</td>
<td>Sepsis/MOF</td>
<td>A-V fistula</td>
<td>0</td>
<td>53</td>
<td>Local</td>
<td>5</td>
<td>Sepsis</td>
</tr>
<tr>
<td>10</td>
<td>14/F</td>
<td>SS</td>
<td>Renal abscess</td>
<td>Drainage</td>
<td>6</td>
<td>90</td>
<td>Inhale</td>
<td>8</td>
<td>DTR, severe anemia</td>
</tr>
<tr>
<td>11</td>
<td>32/M</td>
<td>S/F</td>
<td>Liver disease, Bili 30, sepsis</td>
<td>Cholecystectomy</td>
<td>18</td>
<td>—</td>
<td>Local</td>
<td>2</td>
<td>Intra-abdominal hemorrhage</td>
</tr>
<tr>
<td>12</td>
<td>24/F</td>
<td>SS</td>
<td>MV replacement</td>
<td>RH catheter</td>
<td>0</td>
<td>17</td>
<td>Local</td>
<td>1 (38)</td>
<td>MV rupture</td>
</tr>
</tbody>
</table>

Abbreviations: DIC, disseminated IV coagulation; ARF, acute renal failure; DOA, dead on arrival; MOF, multiorgan failure; TB, tuberculosis; ARDS, adult respiratory distress syndrome; CRF, chronic renal failure; DTR, delayed transfusion reaction; PRBC, packed RBCs; MV, mitral valve; CHF, congestive heart failure.

### Table 2. Profile of Six Surgical Procedures

<table>
<thead>
<tr>
<th>Cholecystectomy and Splenectomy</th>
<th>Dilation and Curettage</th>
<th>Cesarean Section and Hysterectomy</th>
<th>Tonsillectomy and Adenoidectomy</th>
<th>Hip Replacement, Revision, and Prosthesis Removal</th>
<th>Myringotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SS</td>
<td>SC</td>
<td>SS</td>
<td>SS</td>
<td>SS</td>
<td>SS</td>
</tr>
<tr>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Low</td>
<td></td>
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<tr>
<td>Risk level</td>
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<tr>
<td>Mean age (yr)</td>
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<tr>
<td>Age range (yr)</td>
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<tr>
<td>Emergent (%)</td>
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<tr>
<td>Preoperative transfusion (%)</td>
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<tr>
<td>Peroperative transfusion (%)</td>
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</tr>
<tr>
<td>General anesthetic (%)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Postoperative complications</td>
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<tr>
<td>SCD-related (%)</td>
<td></td>
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<tr>
<td>Non-SCD-related (%)</td>
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<tr>
<td>Other (%)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Any complications (%)</td>
<td></td>
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</tbody>
</table>

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Among preoperatively transfused SS patients, the risk of postoperative painful crisis decreased with increasing levels of Hb A ($P = .054$). The mean Hb A percentage in those without pain (N = 161) was 54.8% ± 23.3%, compared with 34.7 ± 29.5% in those with pain (N = 6). However, among all SS patients (transfused and untransfused), total Hb concentration did not differ for those with and without postoperative painful crisis.

There was no association between the development of postoperative ACS in preoperatively transfused SS patients and the mean Hb A percentage ($P = .854$). However, the total Hb concentration of 7 SS patients with postoperative ACS was significantly lower than that of 205 SS patients without ACS (9.3 ± 2.3 vs. 11.1 ± 2.1 g/dL, $P = .024$), even after adjustment for age. The risk of postoperative ACS increased as total Hb concentration decreased (estimated odds ratio, 1.7 times increased risk of ACS with each 1 g/dL, $P = .016$).

**Dilation and curettage.** Only 44% of 70 SS patients and 7% of 14 SC patients received blood transfusion. There was no difference in the overall rate of postoperative complications in SS patients by transfusion status (23.7% of N = 38 untransfused vs. 32.3% of N = 31 transfused, $P = .662$). Except for 2 patients who developed ACS (1 patient was transfused and the other not), all SCD-related complications in SS and SC patients were painful crisis. The most common non-SCD-related complications in SS patients were fever and infection; none was reported in SC patients.

**Cesarean section and hysterectomy.** These procedures were analyzed together. Cesarean sections comprised 55 of the 65 SS procedures (85%) and 16 of the 18 SC procedures (89%). The mean patient age was 25.3 ± 5.3 years for Cesarean section and 32.7 ± 7.9 years for hysterectomy. Seventy-three percent of the Cesarean sections were emergent. Ninety-one percent of the SS and 72% of the SC patients were transfused. The postoperative complication rates were high (42% for SS patients and 50% for SC patients). Although only 6 SS patients were untransfused, the overall complication rate in SS patients did not differ by transfusion status (44.1% of transfused vs. 16.7% of untransfused, $P = .793$). The mean total Hb concentration of all SS patients was not associated with the presence or absence of postoperative complications ($P = .836$).

**Tonsillectomy and adenoidectomy.** All 7 SC patients and 83% of the 35 SS patients were transfused. Postoperative complication rates were fairly low (6% for SS and 14% for SC patients), with no SCD-related complications in SS patients. The postoperative complication rates were similar in transfused (N = 29) and untransfused (N = 6) SS patients (3.5% of transfused vs. 16.7% of untransfused, $P = .318$).

**Hip replacement, revision, and prosthesis removal.** Thirty-four patients were preoperatively transfused, and one was transfused during the intraoperative period. The rate of non-SCD-related complications was 15% for SS and 29% for SC patients. The only SCD-related complication was painful crisis in 1 SS patient. The mean Hb A percentage was 55.3% ± 20.6% with no postoperative complications (N = 26) and 69.6% ± 9.8% with postoperative complications (N = 5; $P = .142$) among the preoperatively transfused SS patients.

**Myringotomy.** Three SC patients and 26 SS patients underwent myringotomy. One SC patient and 54% of the SS patients were transfused. There was one SCD-related complication, ie, a cerebrovascular accident in a chronically transfused SS patient with previous CVA. Non-SCD-related complications (fever and bleeding) occurred in 2 other SS patients (8%). There was no association between the overall postoperative complication rate and transfusion status.

**Anesthesia and Postoperative Complications.** For the low-risk surgical procedures, 73.8%, 10.6%, and 15.6% were performed under general, regional, and local anesthesia, respectively. For the moderate-risk procedures, 93.0%, 6.1%, and 1.0%, were performed under general, regional, and local anesthesia, respectively. Thirteen of the 15 high-risk surgical procedures were performed under general (86.7%) and 2 were performed under local anesthesia (drainage of a brain abscess and cardiac catheterization followed by balloon valvuloplasty). The anesthetic data on 45 surgical procedures (4.2%) were incomplete and excluded from analysis. The effect of type of anesthesia on postoperative complication rates was examined with adjustment for Hb phenotype, age, surgery risk level (low vs. moderate), and transfusion status. Crude postoperative complication rates for SS patients are displayed in Fig 1.

**Non-SCD-related complications.** The most common non-SCD-related postoperative complication was fever. There was a marginally significant effect of anesthesia on non-SCD-related postoperative complication rates ($P = .095$). This effect was similar for SS and SC patients ($P = .199$). These complication rates were lower for surgical procedures with general anesthesia compared with those with regional anesthesia (estimated odds ratio, 0.58; $P = .095$) and compared with those with local anesthesia (estimated odds ratio, 0.51; $P = .100$).

**SCD-related complications.** Painful crisis was the most common SCD-related postoperative complication. Among SS patients, the complication rate was associated with type of anesthesia ($P = .030$), and rates were higher for surgical procedures with regional anesthesia compared with those with general anesthesia (estimated odds ratio, 2.32; $P = .058$) and with those with local anesthesia (estimated odds ratio, 4.65; $P = .014$). Among SC patients, complication rates after general versus regional anesthesia did not differ ($P = .551$), but this may be due to the small number of SC patients who received regional anesthesia (N = 18).

**Perioperative Transfusion and Postoperative Complications.** The effect of blood transfusion on postoperative complication rates was examined with adjustment for Hb phenotype, age, surgery risk level (low vs. moderate), and type of anesthesia. Tables 3 and 4 present postoperative complication rates by surgical risk level and perioperative transfusion status. There were no complications in the 3 SC patients (2 transfused and 1 untransfused) undergoing high-risk surgery (not shown in Table 4).

**Non-SCD-related complications.** For non-SCD-re-
lated postoperative complications, the effect of transfusion depended on both surgery risk level and phenotype \((P = .015)\). There was a significant effect of transfusion only in SC patients undergoing low-risk procedures. When perioperatively transfused, these patients had higher rates of postoperative complications than did untransfused patients \((P = .004)\). The crude rates of non–SCD-related postoperative complications were 28.1% for surgical procedures with perioperative transfusion and 2.1% for those without.

**SCD-related complications.** For SS patients undergoing

### Table 3. Postoperative Complication Rates by Perioperative Transfusion Status SS Surgeries

<table>
<thead>
<tr>
<th>Postoperative Complications (%)</th>
<th>Low-Risk</th>
<th>Moderate-Risk</th>
<th>High-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No TX (N = 145)</td>
<td>TX (N = 248)</td>
<td>No TX (N = 43)</td>
</tr>
<tr>
<td>Pain</td>
<td>12.4</td>
<td>4.4</td>
<td>2.3</td>
</tr>
<tr>
<td>ACS</td>
<td>1.4</td>
<td>0.8</td>
<td>2.3</td>
</tr>
<tr>
<td>CVA</td>
<td>0.0</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Any SCD complications</td>
<td>12.9</td>
<td>4.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Non-ACS infection</td>
<td>2.0</td>
<td>3.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Fever</td>
<td>6.2</td>
<td>8.9</td>
<td>11.6</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.7</td>
<td>2.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Embolism</td>
<td>0.0</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Death</td>
<td>1.4</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Any non-SCD complications</td>
<td>8.8</td>
<td>11.6</td>
<td>14.0</td>
</tr>
<tr>
<td>Other</td>
<td>1.4</td>
<td>5.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Any postoperative complications</td>
<td>18.6</td>
<td>17.3</td>
<td>18.6</td>
</tr>
</tbody>
</table>

Of the SS surgeries, 4 low-risk and 2 moderate-risk surgeries are missing a response to the postoperative complication question.
low-risk surgical procedures, there was a beneficial effect of transfusion (estimated odds ratio for untransfused vs transfused, 3.28; P = .006) on SCD-related postoperative complications, particularly painful crisis. The crude complication rates for SS patients undergoing low-risk surgical procedures were 12.9% for surgical procedures without transfusion and 4.8% for those with transfusion. Accordingly, the mean total Hb concentration of transfused patients was significantly higher (10.3 ± 2.3 g/dL) than that of untransfused patients (8.4 ± 1.3 g/dL; P = .0001). However, among SS patients undergoing moderate-risk surgical procedures, no association was found between transfusion and SCD-related postoperative complications (P = .551). Mean total Hb concentrations of SS patients undergoing moderate-risk surgical procedures were similar for those with and without postoperative painful crisis (10.6 ± 1.9 vs 10.5 ± 2.3 g/dL; P = .883). In contrast, the mean total Hb of 12 SS patients who developed ACS was 9.3 ± 2.0 g/dL, compared with 10.5 ± 2.3 g/dL for 413 SS patients who did not develop postoperative ACS (P = .055). However, this difference did not remain after adjusting for age.

Among SC patients there was a beneficial effect of perioperative transfusion regardless of surgery risk level (estimated odds ratio for untransfused vs transfused, 8.33; P = .009). The crude rate of complications after low- and moderate-risk surgeries was 2.5% with perioperative transfusion and 11.6% without. The mean total Hb concentration was 11.3 ± 1.6 g/dL for untransfused SC patients and 12.0 ± 2.3 g/dL for perioperatively transfused SC patients. Notably, 3 of 21 untransfused SC patients undergoing moderate-risk surgical procedures had ACS, but none of the 49 transfused patients in this group did.

Sβ0 Thai and Sβ+ Thai Patients

Fifty-two surgical procedures were performed on 41 Sβ0 Thai patients. There were 11 cholecystectomies, 5 splenectomies, 2 hip replacements/revisions, 8 dilation and curettage procedures, 4 circumcisions, 2 laparotomies, 2 laparoscopic evaluations, 2 tubal ligations, 1 Cesarean section, 1 tonsillectomy, 1 adenoectomy, and 13 other surgical procedures. The SCD-related postoperative complication rate was 9.6% (3 painful crises, 1 ACS, and 1 with both). The non-SCD-related complication rate was 11.5%.

Thirteen of 16 Sβ+ Thai patients were perioperatively transfused for cholecystectomy or splenectomy (81.3%). Of these transfused patients, 1 patient had fatal postoperative bleeding, and another had a painful crisis, ACS, fever, and thrombosis after the surgical procedure. No complications were reported for the 3 untransfused patients.

Twenty-nine surgical procedures were performed on 21 Sβ+ patients. There were 2 splenectomies, 3 Cesarean sections, 5 tonsillectomies, 5 dilation and curettage procedures, 2 inguinal hernia repairs, 1 myringotomy, 1 hip revision, and 13 other surgical procedures. The perioperative transfusion rate was 41.4%. The only SCD-related postoperative complication was 1 ACS event after splenectomy with intraoperative transfusion (preoperative total Hb, 13.2 g/dL). No non-SCD-related complications were reported.

DISCUSSION

Because previous studies have shown significant complications for SCD patients undergoing surgical procedures, most centers follow protocols for use of perioperative preparative transfusion, and only a few investigators have reported a paucity of morbidity data in untransfused patients undergoing minor procedures. These increased risks are believed to be secondary both to acute tissue injury and chronic organ damage produced by vaso-occlusion from sickled red blood cells (RBCs). In addition, surgical procedures may be complicated by hypoxia, acidosis, or hypothermia, adding to a greater likelihood of SCD patients experiencing an adverse event, because each of these factors promotes erythrocyte sickling. Although RBC transfusions have been advocated by many investigators to reduce perioperative complications, there are no controlled trials documenting their benefit. There are also significant risks associated with RBC transfusions, including alloimmunization and exposure to infectious diseases.

The CSSCSD was designed to define the natural history of SCD and its effects on health events. The recruitment procedures insured that participants were representative of the wide spectrum of clinical severity that is a hallmark of this disease. Because this unique population was observed prospectively for a median of 6 years, it is ideally suited to define the types of surgical procedures and associated complications that can be observed in patients with SCD.

There were several interesting observations noted in this study. The overall mortality rate was very low (0.3%). There were only 3 deaths attributed to the surgery or anesthesia. No deaths were observed in patients under the age of 14 years, although many children had procedures associated with moderate surgical risk.

The SCD-related complication rates were similar for SC and SS patients undergoing abdominal surgeries and orthopedic procedures. The level of Hb A in the transfused pa-
tients did not decrease postoperative complication rates, except for the decrease in the rate of postoperative pain crisis for abdominal surgeries. There were only 21 procedures among Sβ0 that patients enrolled in the study, and there was no report of cholecystectomy. Although the total number of patients was small, this low number of surgeries may be reflective of the more benign phenotype.

There was wide variation in the SCD-related complications associated with the more common surgeries. The rate for SS patients was 0% for tonsillectomy and adenoidectomy, 2.9% for hip surgery, 3.9% for myringotomy, 7.8% for intra-abdominal surgery, 16.9% for cesarean section and hysterectomy, and 18.6% for dilation and curettage. Reasons for this wide variation were not identified, although the high rate of sickle cell complications after Cesarean section probably is related to the increased morbidity associated with pregnancy in women with sickle cell anemia irrespective of transfusion practices. At present, because laparoscopic cholecystectomy has replaced the open procedure, the duration of hospitalization, transfusion requirements, and postoperative complications will most likely be lower than that reported here.

We also observed that in the patients transfused before intra-abdominal surgery, the mean level of Hb A was higher for those patients with no painful crisis compared with those who experienced painful crisis after surgery (58% vs 35%, respectively). However, prevention of painful crisis in the postoperative period does not alone justify the use of preoperative transfusions in light of the recognized complications of blood transfusion. The recently concluded randomized controlled trial evaluating perioperative blood transfusion has defined the role of preoperative blood transfusion for sickle cell patients.

This study also showed that non-SCD complication rates for fever and infection were higher in patients receiving regional anesthesia compared with those who had received general anesthesia but unrelated to the preoperative transfusion rates. Because regional anesthesia (specifically epidural) is commonly used in Cesarean sections and other assisted deliveries, the higher complication rates observed may be a reflection specifically of the higher complication rates observed in those obstetrical procedures.

In non-SCD patients undergoing surgery, perioperative complications vary from general pulmonary complications of 3% to 70% to serious ACS-like events of less than 1%. Similarly, in-hospital complications for open cholecystectomy occur in 22.4% (unadjusted rate) of patients. Our data show that SCD patients are at no greater risk for these complications than the non-SCD patients.

Although not derived from a rigorously controlled trial, the data do define the types of commonly performed surgeries on patients with SCD and provide new insights into postoperative complications. Despite the variety of techniques used to manage patients and the variations in methods of inducing anesthesia, mortality was low and there were relatively few serious perioperative complications related to SCD. In part, this outcome can be attributed to careful attention to the details of patient management by the collaborative efforts of the hematologist, surgeon, and anesthesiologist. However, the role of transfusion in the perioperative period remains to be defined, but the data do suggest that not all patients undergoing surgery should routinely receive blood transfusions.

During the study period, no protocol was specified for preoperative transfusion practice. Each center continued to follow its own preoperative preparatory regimen. The patient’s age, disease state, multiorgan disease status, and American Surgical Association (ASA) risk level were not predetermined.

For the minor procedures, many of the patients did not receive blood transfusions and complication rates were low. The postoperative complication rates were also low for the 42 patients who underwent tonsillectomy. Six SS patients who were untransfused had no complications after tonsillectomy. The paucity of complications after this procedure may be related to the younger age of patients at the time of surgery.

Recent advances in intraoperative techniques and new anesthetic agents have been touted for successful outcomes for SCD patients in postoperative periods, rather than the use of blood transfusion regimen alone. Others credit aggressive preoperative transfusion preparation as responsible for the successful outcome of SCD patients undergoing surgical procedures. The percent reduction of S Hb required for transfusing patients is not well defined in those receiving mandatory preoperative transfusion.

Surgical procedures can be performed successfully on SCD patients. Careful assessment of Hb phenotype, past medical history, and risk status should be documented.

Blood transfusion therapy will continue to be part of the preoperative evaluation and preparation of patients. Simple transfusion to increase the Hb level to 10 g/dL, blood replacement for profound anemia of Hb less than 5 g/dL, and intraoperative hemorrhage appears appropriate. Transfusion still carries with it the complications of alloimmunization, delayed transfusion reaction, transmission of viral infection, hepatitis, and iron overload. These complications should be considered when counseling patients and family before the surgical procedure.

ACKNOWLEDGMENT

The authors are indebted to Pamela Moore, Shaheen Islam, and Susan Wester for their assistance in preparing this manuscript. The following were senior investigators in the CSSC: Clinical centers: R. Johnson, Alta Bates Hospital (Berkeley, CA); L. McMahon, Boston City Hospital (Boston, MA); O. Platt, Children’s Hospital (Boston, MA); F. Gill and K. Ohene-Frempong, Children’s Hospital (Philadelphia, PA); G. Bray, J. Kelleher, and S. Leikin, Children’s National Medical Center (Washington, DC); E. Vichinsky and B. Lubin, Children’s Hospital (Oakland, CA); A. Bank and S. Piomelli, Columbus Presbyterian Hospital (New York, NY); W. Rosse, J. Falletta, and T. Kinney, Duke University (Durham, NC); L. Lessin, George Washington University (Washington, DC); J. Smith and Y. Khakoo, Harlem Hospital (New York, NY); R. Scott, O. Castro, and C. Reirdorf, Howard University (Washington, DC); D. Doak, S. Diamond, and R. Bellevue, Interfaith Medical Center (Brooklyn, NY); W. Wang and J. Wilmus, LeBonheur Children’s Hospital (Memphis, TN); P. Milner, Medical College of Georgia (Augusta, GA); A. Brown, S. Miller, R. Riedel, and P. Gillette, State University of New York Health Science Center at Brooklyn (Brooklyn, NY).

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RISKS OF SURGERY AND ANESTHESIA IN SICKLE CELL DISEASE


APPENDIX

Description/location of 1,079 surgical procedures. Two hundred twenty-two cholecystectomy, 2 cholecystotomy, 3 obstruction of gall bladder, 36 splenectomy, 107 dilation and curettage for pregnancy termination and miscellaneous complications, 7 dilation and curettage postpartum and for ectopic pregnancy, 75 Cesarean section, 12 hysterectomy, 46 tonsils and adenoids, 21 hip replacement, 19 hip revision, 3 hip prosthesis removal, 30 myringotomies, 5 craniotomy, 4 spinal canal, 4 miscellaneous nervous system, 6 retina, 4 scleral buckling, 12 miscellaneous eye, 1 myringoplasty, 1 tympanoplasty, 2 radical mastoidectomy, 3 sinus, 11 dental extraction and restoration, 2 cleft palate correction, 5 bronchial and pulmonary biopsy, 6 miscellaneous respiratory, 20 vascular access, 7 miscellaneous cardiovascular, 5 lymphatic node biopsy, 10 appendectomy, 3 hemorrhoidectomy, 16 inguinal hernia repair, 8 umbilical hernia repair, 19 laparotomy and laparoscopy, 5 miscellaneous digestive system, 3 kidney transplant, 10 miscellaneous urinary system, 4 undescended testes, 6 penile prosthesis, 17 priapism surgery, 22 circumcision, 4 miscellaneous male genital organ, 4 ovaries and Fallopian tubes, 20 tubal ligation, 3 breast reduction/enhancement, 8 miscellaneous breast surgery, 6 miscellaneous gynecological, 8 incision and drainage of long bones, 5 osteotomy, 18 bone excision and biopsy, 5 bone graft, 8 open reduction and treatment of fractures, 4 joint fusion, 2 shoulder and wrist replacement, 4 clubfoot release, 6 tendon and sheath repair, 12 miscellaneous musculoskeletal, 31 skin debridement, 21 skin and subcutaneous, 38 skin graft, 2 parathyroidectomy, 49 diagnostic procedures.

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