# Comparative Effectiveness of Different Types of Splenectomy for Children with Congenital Hemolytic Anemias

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**Objective** To compare the effectiveness of different types of splenectomy in children with congenital hemolytic anemias.

**Study design** We constructed key questions that addressed outcomes relevant to clinicians and families on effects of partial or total splenectomy, including hematologic effect, splenic function, and the risk of adverse events. We identified from Pubmed and Embase 703 studies that evaluated different types of splenectomy and accepted 93 studies that satisfied entry criteria. We graded the quality of each report and summarized the overall strength of research evidence for each key question.

**Results** We did not identify any randomized clinical trials. All types of splenectomy have favorable clinical outcomes in most diseases. We did not identify any hematologic advantage of laparoscopy compared with laparotomy. Adverse events are uncommon in most studies and are minimized with use of laparoscopy.

**Conclusions** There is a need for randomized clinical trials and improved data collection of different types of splenectomy in congenital hemolytic anemias. Outcomes studied should address the concerns of families and clinicians to assess the risks and benefits of various treatments. *(J Pediatr 2012;160:684-9)*.

For children with congenital hemolytic anemias (CHA) such as sickle cell disease (SCD), thalassemias, and hereditary spherocytosis (HS), a splenectomy can control hemolysis and sequestration crises.[1] However, the use of total splenectomy is limited by risks of overwhelming postsplenectomy sepsis, vascular thrombosis, and pulmonary hypertension.[2] Although partial splenectomy has been increasingly used for CHA, the efficacy of partial compared with total splenectomy is unclear. Similarly, the advantages of laparoscopy compared with laparotomy are not defined. The purpose of this review is to compare the effectiveness of different types of splenectomy for children with CHA, such that clinicians and families are informed about the evidence about management.

## Methods

This report is a product of a research consortium titled Splenectomy in Congenital Hemolytic Anemia, which is composed of pediatric surgeons, pediatric hematologists, and informatics experts (**Appendix 1**; available at www.jpeds.com). This report was based on the framework of the US Agency for Healthcare Research and Quality.[3] We first identified key questions that reflect issues relevant for families and clinicians: (1) What is the evidence of the effectiveness of different types of splenectomy for improving hematologic outcomes in children with CHA?; (2) What is the evidence of the effectiveness of different types of splenectomy on splenic function in children with CHA?; and (3) What are the adverse events associated with different types of splenectomy for children with CHA?

We searched PubMed and Embase (1990-April 2011) for English language and human studies with medical subject headings (MeSH) terms (inclusive) of: splenectomy, partial splenectomy, CHA, HS, and sickle cell anemia. Studies were limited to those reporting on children <18 years of age (full search in **Appendix 2**; available at www.jpeds.com). Splenectomy in Congenital Hemolytic Anemia Consortium members provided additional references.

Abstracts identified from the primary search were reviewed for inclusion by all authors. When at least one author considered the abstract relevant, the full-text article was reviewed. Reports of splenectomy for other diseases, such as trauma, idiopathic thrombocytopenia purpura, or

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| ACS | Acute chest syndrome |
| CHA | Congenital hemolytic anemias |
| DA | Dyserythropoietic anemia |
| Hgb | Hemoglobin |
| HJB | Howell-Jolly bodies |
| HS | Hereditary spherocytosis |
| MeSH | Medical subject headings |
| RBC | Red blood cell |
| SCD | Sickle cell disease |

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malignancy, were excluded. Studies on angiography or splenic auto-transplantation were excluded, because these options do not represent common practice. We excluded studies reported in abstract form only or that reported <5 children.

### Outcomes of Interest

For question 1, outcomes included: (1) hemoglobin; (2) reticulocyte count; (3) rate of anemic or sequestration crises; or (4) transfusions. For question 2, outcomes included clearance of Howell-Jolly bodies (HJB), pitted red blood cell (RBC) count, radionuclide liver-spleen scan, or laboratory studies. For question 3, outcomes included the rate of perioperative (<30 days postoperatively) and long-term (>30 days) adverse events, including death, infection, bleeding, intraoperative conversion from laparoscopy to laparotomy or from partial splenectomy to total splenectomy, and other adverse events relevant to this population, such as acute chest syndrome (ACS), vascular complications, rate of total splenectomy after earlier partial splenectomy, length of stay, and pain. We identified use of standardized definitions of adverse events, such as those from National Surgical Quality Improvement Program-Pediatrics.[4]

### Quality Assessment

For questions 1 and 2, the methodological quality of each study was graded on the basis of the US Agency for Healthcare Research and Quality criteria.[3] This grading assessed 4 domains: risk of bias, consistency, directness, and precision. The risk of bias was assigned as low, medium, or high on the basis of assessment of study design and extent to which outcomes were described. Consistency was assigned as consistent or inconsistent on the basis of assessment of the degree of similarity in outcomes and effects. Directness was assigned as direct or indirect on the basis of assessment of whether the evidence was causally linked to the outcome of interest. Precision was assigned as precise or imprecise on the basis of assessment of the confidence in reported outcomes on the basis of research methods, including statistical analysis.

On the basis of domain assessments, each study was assigned an overall quality grade of A, B, or C.[3] The final grade represents a consensus opinion of the authors. Category A studies have the least bias and are considered valid. These studies include rigorously conducted randomized clinical trials, clear description of population and interventions, appropriate analyses, and minimal bias. Category B studies are susceptible to some bias and do not meet all the criteria of category A. Although deficient in some respects, they are not sufficiently deficient to invalidate results. Category C studies have significant bias that may invalidate results, including serious errors in design, analysis, reporting, and missing substantial data.

### Strength of Evidence Summary

For summary of the strength of evidence, we assigned a rating of high, moderate, low, or insufficient related to each question as follows[3]: (1) High—there is a high level of assurance that the research findings are valid. No important disagreement exists across studies, and at least two A-quality studies are required for this rating; (2) Moderate—there is a moderate level of assurance that the findings are valid, little disagreement exists across studies, and contains A- or B-quality studies that lack long-term outcomes; (3) Low—there is a low level of assurance that the findings are valid, contains studies with conflicting results, including B- or C-quality studies; and (4) Insufficient—evidence does not permit estimation of an effect.

## Results

Our primary search yielded 703 citations, with 141 abstracts identified as relevant. After secondary review, 93 studies were included in the final report.[5-97] There were no randomized clinical trials. Our analysis of these studies is organized by question (**Tables I-III**; available at www.jpeds.com) and a summary of evidence (**Table IV**; available at www.jpeds.com).

### Hematologic Outcomes

Of the 53 studies applicable to question 1, 9 compared different types of splenectomy (**Table I**). Overall, there were 2466 subjects, and sample sizes ranged from 5 to 150. No study was graded quality A, 30 studies were graded quality B, and 23 were graded quality C. Follow-up periods ranged from 6 months to 25 years. Results are summarized by disease.

Sixteen studies with a total of 476 subjects reported on HS. Four studies compared different types of splenectomy. Most studies of partial splenectomy reported an increase in hemoglobin level of 2 to 4 gm/dL and a decrease in reticulocytes, transfusions, and anemic crises. Most studies of total splenectomy reported an increase in hemoglobin level of 4 to 5 gm/dL, with a decrease in reticulocytes, transfusions, and anemic crises.

Sixteen studies with a total of 867 subjects reported on SCD. Several studies specified outcomes in different types of SCD, including hemoglobin (Hgb) SS, Hgb SC, and combined Hgb S/ß-thalassemia. For the 13 studies that examined total splenectomy, there was varied effect on hemoglobin, although most studies reported a decrease in sequestration crises. Similarly, for the 3 studies that reported the use of partial splenectomy, there was varied effect on hemoglobin, but a decrease in sequestration events.

Nine studies with a total of 488 subjects examined outcomes in thalassemias. Five studies compared different types of splenectomy. Overall, these studies showed a varied effect on hemoglobin, but a marked decrease in transfusions.

Eight studies with a total of 560 subjects reported different types of splenectomy, which analyzed outcomes in cohorts including multiple types of CHA. Outcomes of combined Hgb S/ß-thalassemia were included in an earlier discussion of SCD. Because different diseases were grouped the interpretation of findings was limited, but most reports showed a rise in hemoglobin level and a decrease in reticulocyte, transfusions, and anemic/sequestration crises.

Four studies with a total of 65 subjects identified other types of CHA. Durakbasa et al reported a complete response to total splenectomy in dyserythropoietic anemia (DA) and no