Splenectomy in sickle cell disease: do benefits outweigh risks?

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The spleen is one of the first organs to be damaged in sickle cell disease (SCD). The unique environment of the spleen is particularly challenging for SCD erythrocytes, with constant intrasplenic sickling and trapping of erythrocytes in the red pulp causing repeated splenic injury from a very young age.[1] This process is clinically silent in most children, manifesting mainly as progressive functional asplenia with a high risk of invasive bacterial infections,[2-4] a complication that can be managed with daily prophylactic penicillin and appropriate immunizations. Nonetheless, some children with SCD experience other serious clinical complications related to the spleen, including acute splenic sequestration and chronic hypersplenism.[1]

Acute splenic sequestration is an unpredictable and life-threatening complication particularly affecting young children with HbSS. Resulting from acute trapping of blood in the spleen caused by sudden enhanced intrasplenic sickling, symptoms include rapid splenic enlargement with acute anemia and potentially hypovolemia. Estimated rates of acute splenic sequestration vary according to age and sickle cell genotype. In HbSS, the first episode typically occurs between 6 months and 5 years of age, most within the first 2 years of life.[5,6] After one episode of acute splenic sequestration, 67% of children with HbSS will experience a recurrent episode.[5] In other SCD genotypes, such as HbSC disease and HbS/β^+-thalassemia, acute splenic sequestration is more often reported in older children and young adults.[7] Acute splenic sequestration is typically treated with blood transfusions and surgical splenectomy is often recommended for children with recurrent episodes.[8,9] Another clinical indication for surgical splenectomy in SCD is hypersplenism. Persistent splenic enlargement is likely due to chronic intrasplenic erythrocyte sequestration and may be accompanied by low hemoglobin concentration, thrombocytopenia, and leukopenia, as well as abdominal pressure from the spleen and failure to thrive.

The benefit/risk ratio of splenectomy is particularly complex in SCD. On the one hand, surgical splenectomy provides an immediate clinical benefit in children with recurrent acute splenic sequestration or severe hypersplenism. On the other hand, splenectomy may be associated with both short- and long-term surgical, septic, and thromboembolic risks which are not fully understood nor evaluated. Additionally, most children with SCD become functionally asplenic at a very young age, adding to the complexity of a surgical risk evaluation as outcomes on morbidity and mortality related to the spleen are very difficult to interpret.

In a Letter to the Editor published in this issue of *Haematologica*, Pinto *et al.*[10] compared survival and long-term complications in splenectomized and non-splenectomized individuals with SCD in Italy. Presenting retrospective data from 534 individuals with SCD, 117 (32%) of whom had undergone surgical splenectomy, the study provides novel evidence on the absence of long-term increased mortality related to surgical splenectomy in SCD. With a median follow-up of 26 years, this study is the first to provide such reassuring long-term post-splenectomy follow-up data. However, some important study features must be considered when extrapolating results to other clinical settings, particularly if they are to be used as guidance for clinical decision-making.

The study included individuals with various genotypes reflecting the specific epidemiology of SCD in Italy: 32% had HbS/β^+-thalassemia, 33% had HbS/β^0-thalassemia, and only 35% had HbSS. The rate of surgical splenectomy varied significantly between these three genotypes, with as many as 53.4% of individuals with HbS/β^0-thalassemia and 33.9% of individuals with HbS/β^+-thalassemia having undergone surgical splenectomy, compared to just 9.6% of individuals with HbSS. Furthermore, the median age at splenectomy was 7 years in the HbSS group compared to 11 years in the HbS/β^0-thalassemia group and 20 years in the HbS/β^+-thalassemia group. Hypersplenism/recurrent splenic sequestration was the indication for splenectomy in 68.8% of patients, a percentage reflecting the high proportion of patients with HbS/β^0-thalassemia and

HbS/β⁺-thalassemia. Findings may therefore not accurately capture the risks of surgical splenectomy when performed in young children with HbSS, which is likely the majority of children requiring surgical splenectomy in many settings.[11]

The study found no difference in the rate of fatal infectious complications between splenectomized and non-splenectomized individuals. This is not surprising for children with HbSS or HbS/β⁰-thalassemia who are known to become functionally asplenic in early childhood, thus rendering them highly susceptible to invasive bacterial infections regardless of whether they undergo surgical splenectomy or not.[2-4] In contrast, splenic dysfunction in HbS/β⁺-thalassemia has not been widely evaluated, and for this group of patients the findings presented in this study are particularly valuable.

A relationship that is not as well understood in SCD is the association between splenectomy (autosplenectomy or surgical splenectomy) and thromboembolic risk. This study did not demonstrate any specific risks of long-term thromboembolic complications.

There is a general paucity of research on the spleen in SCD. Although the study by Pinto *et al.*[10] provides much needed novel evidence on the absence of long-term mortality related to surgical splenectomy, data on potential benefits of splenectomy are still sparse. Overall, international guidelines on the management of acute splenic sequestration and hypersplenism are lacking and recommendations for surgical splenectomy are based on weak evidence and pertain to all types of SCD despite genotypic variations in age and clinical presentation.[8,9] Splenic complications in SCD are common and associated with high morbidity and mortality. Multicenter studies addressing parameters for and timing of surgical splenectomy, considering different genotypes, baseline splenic function and the variability in clinical settings, are necessary in order to provide adequate clinical guidelines and optimal care for all children and adults living with SCD.

Disclosures

No conflicts of interest to disclose.

Contributions

AN-M and VB co-wrote this editorial.

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