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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 immunisations. Nonetheless, some children with SCD experience other serious clinical complications related to the spleen, including acute splenic sequestration (ASS) and chronic hypersplenism (1).

ASS 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 anaemia and potentially hypovolaemia. Estimated rates of ASS vary according to age and sickle cell genotype. In HbSS, the first episode typically occurs between six months and five years of age, most within the first two years of life (5, 6). After one episode of ASS, 67% of children with HbSS will experience a recurrent episode (5). In other SCD genotypes, such as HbSC-disease and HbS/β-thalassaemia, ASS is more often reported in older children and young adults (7). ASS 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 haemoglobin 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 one hand, surgical splenectomy presents an immediate clinical benefit in children with recurrent ASS 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 splenectomised and non-splenectomised individuals with SCD in Italy. Presenting retrospective data from 534 individuals with SCD, 117 (32%) of which 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 time 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+thalassaemia, 33% had HbS/β0-thalassaemia, 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/β0-thalassaemia and 33.9% of individuals with HbS/β+-thalassaemia 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/β0-thalassaemia group and 20 years in the HbS/β+-thalassaemia 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/β0-thalassaemia and HbS/β+-thalassaemia. 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 splenectomised and non-splenectomised individuals. This is not surprising for children with HbSS or HbS/β0-thalassaemia 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+-thalassaemia has not been widely evaluated, and for this patient group 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 ASS 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. Multicentre 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 living with SCD.
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