Near-Total Splenectomy

A New Technique for the Management of Hereditary Spherocytosis

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Objective: The authors used a new surgical technique of near-total splenectomy (NTS) and report their experience.

Summary Background Data: Total splenectomy is indicated for the management of patients with hereditary spherocytosis but may be complicated by severe infections and thromboembolic events. Studies have shown that partial or subtotal parenchymal resections can lead to excessive regeneration of the residual parenchyma. The resulting onset of hemolysis requires total splenectomy in a significant portion of patients. Our hypothesis was that a more radical approach to open resection permanently decreases recurrent hemolysis while potentially ensuring immune function.

Methods: This longitudinal cohort study included 42 patients with moderate to severe hereditary spherocytosis who underwent NTS according to an open procedure developed by the authors. The end criterion was to conserve a remnant spleen of 10 cm^3 in size.

Results: Patient age ranged between 2 and 42 years. Mean resected spleen weight was 580 g; mean remnant volume was 10 cm^3 (range, 8–11 cm^3). A surgical complication (loss of spleen) occurred in 1 patient. Six-month to 6-year follow-up data was available on 22 patients; 21 of 22 showed preserved phagocytosis and normal blood circulation of the remnant; 1 of 22 experienced secondary remnant necrosis. On average, the remnant spleen grew back to four and a half times its postoperative size. No patients required transfusions, developed gallstones, or symptomatic hemolysis.

Conclusions: This new technique of NTS is safe, effective, and can minimize the late sequelae of secondary splenectomy.

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Elective splenectomy in patients with hereditary spherocytosis (HS) is the surgical treatment of choice.[1,2] Previously, total splenectomy was recommended in patients with HS with moderate or severe hemolytic anemias, a recurrent need for transfusions, and/or reduced physical ability (Table 1). Loss of the spleen, however, leads to a lifelong higher risk for sepsis and severe infection[1,3–7] and may be associated with an increased rate of thromboembolic complications,[8] enhanced arteriosclerosis, and late coronary heart disease.[9]

In most patients, the anatomic structure of the spleen along the craniocaudal axis shows a division into 2 to 3 lobes and 3 to 5 segments. The transverse plane is divided into peripheral, intermediate, and hilar zones.[10] In most cases, the splenic artery diverts distant from the hilus into the segmental arteries, which subsequently form the arch of the splenic artery. Vascular dissection is more difficult when the arteries divide close to the hilus. Three compartments are distinguished according to structural and functional criteria.[10–12]

Red pulp acts like a "blood filter" providing splenic clearance of encapsulated bacteria, blood parasites, and other antigens by phagocytosis. Another function is "pitting," or the milking out of nuclear fragments (Howell-Jolly Bodies) or membrane inclusions from erythrocytes (pocked or pitted cells).[13] Their levels in the blood are markedly increased after total splenectomy. The *white pulp* plays a key role in lymphocyte recirculation with memory B lymphocyte- and antibody-producing cells.

The *marginal zone* is a center for maturation of the $CD21^+$ B-cells, which recognize antigens independently of T-cell function. The loss of production of specific antibodies critically affects the immune defense against encapsulated bacteria such as pneumococci, meningococci, and *Haemophilus influenzae* type B. Spleen removal results in reduced specific antibody production. Immaturity of the marginal zone in patients under the age of 6 years explains toddlers' increased susceptibility to infections.

Surgical procedures aimed at sparing part of the spleen may offer an alternative to total splenectomy. Partial or subtotal parenchymal resections have been performed successfully, with preservation of approximately one third to one fourth of the size of an age-related spleen or removal of 80% to 90% of the enlarged spleen[14–17] or leaving a residual parenchyma about the size of a man's fist.[18] However, it has been demonstrated that partial or subtotal splenectomy can

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TABLE 1. Clinical Classification of Hereditary Spherocytosis (HS) and Surgical Indication[2]

	Mild HS	Moderate HS	Severe HS	Very severe HS†
Hemoglobin (g/dL)	11–15	8–11	6–8	< 6
Reticulocytes (%)	3–8	≥ 8	≥ 10	≥ 10
Bilirubin (mg/dL)	1–2	≥ 2	2–3	≥ 3
Spectrin content (% of normal*)	80–100	50–80	40–80[3]	20–60‡
Osmotic fragility				
Fresh blood	Normal or slightly elevated	Markedly elevated	Markedly elevated	Markedly elevated
Incubated blood	Markedly elevated	Markedly elevated	Markedly elevated	Markedly elevated
Splenectomy	Usually not be indicated	Indicated if repeated transfusions required or reduced physical ability	Indicated	Indicated

*Normal (mean ± standard deviation): 226 ± 54 × 10^3 molecules/cell.
†Patient requires regular transfusions.
‡As a result of various primary defects, the spectrin content of erythrocytes varies greatly.

lead to substantial regrowth of the residual spleen back to its original size and renewed onset of hemolysis; in some cases, the remnant spleen had to be removed in total.[14,17,19] Some subtotally splenectomized patients who have had 80% to 90% of their spleen resected experienced pronounced residual spleen growth and developed recurrent hemolysis and required repeat surgery.[14,17]

Other authors performing subtotal resection reported that the remnant spleen will, on average, grow back to its age-equivalent size 2 to 3 years after partial or subtotal splenectomy.[17] After 5 to 6 years, the volume doubled.[17] The revision rate for recurrent hemolysis after the conventional subtotal procedure is estimated to be 10% after 5 years and 33% after 10 years.[17] One study reported a reoperation rate as high as 40%.[14]

Based on these observations, we hypothesized that an even more radical approach than the conventional subtotal resection would achieve a longer lasting reduction of hemolysis while ensuring splenic immunologic and clearance functions. A residual spleen volume of 10 cm^3 appeared to us to be optimal because this volume represents the smallest resectable size in which the spleen survives but the venous backflow remains large enough to prevent thrombosis of the splenic vein. Because circulatory capability is critical to maintaining residual splenic function,[20] perfusion would have to take place through the hilar vessels, not the short gastric arteries.[21] The anatomic preservation of a splenic core transversing all 3 zones would allow compartmental functions to maintain maximum splenic blood flow while ensuring clearance.

In 1995, our hospitals started using a modified form of the Tchernia[16] subtotal technique as the standard surgical management of HS. In 1996, we advanced Tchernia's subtotal splenectomy from 80% to 90% up to 98% removal into a new standardized technique we call near-total splenectomy (NTS). We have performed NTS on 42 patients with HS to date. We now describe our technique and discuss its clinical outcomes.

METHODS

We performed a newly developed surgical technique of NTS on 42 patients with HS.

Patients

Between 1996 and 2002, 42 patients with HS aged 2 to 42 underwent NTS for moderate to severe hereditary spherocytosis. The patients were operated on in the Department of General Surgery, University of Goettingen, Germany (n = 38) and the Department of Surgery, Children's Hospital, University of Zurich, Switzerland (n = 4). The surgical objective was to preserve a residual spleen of 10 cm^3 in size with blood flow through the hilar vessels independent of age, severity of HS, or original spleen size. The patients were required to have been vaccinated against pneumococci, meningococci, and *H. influenzae* type B or were given postoperative booster shots.

Informed consent was obtained from the patients or their legal guardians in accordance with hospital protocol. Since 1995, this modified form of the Tchernia subtotal technique had already been the standard institutional procedure for HS at our hospitals.

Surgical Technique

The patients were positioned in 20° lateral right recumbency with the left arm abducted. Laparotomy was carried out by the subcostal approach, terminating laterally at the

11th intercostal space to present the spleen. After dissection of the lateral gastrocolic and splenorenal ligaments with bipolar or ultrasonic scissors (Ultracision; Ethicon Endo-Surgery, Inc., Cincinnati, OH), the spleen was mobilized from the lateral abdominal wall and the retroperitoneum and then lifted out of the abdominal cavity. This is the point when the surgeon is able to identify which part of the spleen could best be preserved, either the cranial or caudal pole, depending on vessel anatomy. We always preserved the lower part of the inferior splenic pole as a result of its topographic localization and much easier accessibility. We refrained from preserving splenic sections located closer to the hilum because complicated dissection of segmental vessels would pose more difficulty and a greater risk of vascular injury.

The gastrosplenic ligament with its short gastric arteries was separated. The splenic hilus was dissected stepwise in the craniocaudal direction between Overholt clamps and resorbable sutures. Care was always taken to avoid injury to the pancreatic capsule. It was usually possible to preserve the most caudal vessels entering the splenic pole from the direction of the splenic hilus.

Because the objective was to preserve a residual spleen of 10 cm^3 containing all 3 functional parts of the spleen, full-thickness parenchymal resection was accomplished completely inside the perfused spleen segment. A cylinder of tissue (approximately 2 cm in diameter) was excised with the scalpel after temporarily clamping the afferent vessels with a bulldog clamp. Figure 1 diagrammatically illustrates the optimal excision of a cylinder. For this part of the operation, we refrained from using monopolar electrocautery or bipolar scissors to avoid the risk of high-frequency thermal injury to the preserved vessels. This procedure allows conservation of all 3 splenic compartments and the angioarchitecture of the smallest units of the splenic remnant.[11,20]

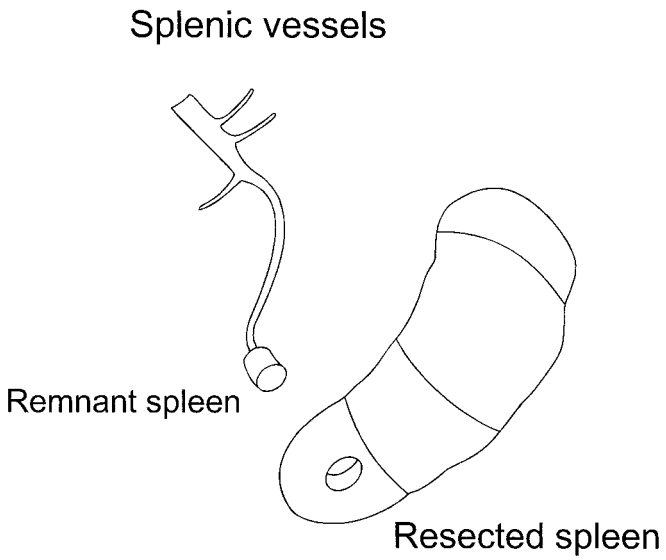

FIGURE 1. Graphic illustration of the cylindrical splenic remnant (10 cm^3, 2 cm in diameter) with its vascular supply.

To prevent bleeding, transected vessels of remnant parenchymal surfaces were localized by intermittently releasing the bulldog clamp and closed by transfixing ligature with 6–0 resorbable monofilament sutures. To avoid parenchymal tears in soft and delicate tissue, the knots in the sutures were tied just tightly enough to achieve hemostasis, but with very little tension. Usually, 6 to 8 transfixing ligatures were required. All exposed surfaces were covered with a native equine collagen fleece (TachoComb H; Nycomed Austria GmbH, Linz, Austria). This ready-to-use fleece is coated with fibrinogen, thrombin, and aprotinin. When the fleece comes into contact with biologic fluids, a durable fibrin clot is formed that seals the fleece tightly to the wound and reliably stops any large-area seeping bleeds. Throughout these manipulations, the preserved vessels must never be pulled on too harshly.

The resected splenic tissue was weighed immediately. To determine the volume of the splenic remnant, it was placed briefly in a vessel completely filled with water. The amount of water displaced by the remnant spleen was used to calculate remnant spleen volume according to Archimedes' principle.

Whenever supernumerary spleens were present, they were always extirpated completely. The residual spleen was positioned in the left upper abdomen without any fixation. Closure of the abdominal wall and skin was performed with resorbable running sutures.

Postoperative Management

Immediately after surgery, continuous intravenous heparinization (150 IU/kg body weight/d) was given up to postoperative day 2 to prevent thrombosis of the splenic vein, followed by a changeover to acetylsalicylic acid (1.5 mg/kg body weight/d) for at least 3 months or for the duration of thrombocytosis (>600,000/μL). On postoperative day 2, the antibiotic therapy parenterally started immediately preoperatively was switched to oral penicillin (Penicillin V, 25,000 IU/kg body weight/d). On the day of surgery, there were no restrictions on oral fluid intake. The patient was allowed to eat a normal diet without additional parenteral substitution and was fully mobilized by postoperative day 1. Before discharge, a Doppler color flow was taken of the preserved splenic vessels.

Follow-up Examinations

Splenic Imaging

Spleen size was determined using a 7.5-MHz curved array transducer (Eccocee; Toshiba, Netherlands) and the 3 organ axes of the remnant spleen were measured by sonog-

raphy. The volume of this prolate ellipsoid having 3 axes was determined using the following formula[22]:

$$V\ (cm^3) = \text{height (cm)} \times \text{width (cm)} \times \text{length (cm)} \times \pi/6$$

Splenic Perfusion/Thrombosis

To rule out thrombosis, Doppler color flow was used to examine blood flow in the splenic artery and vein, both renal veins, the portal vein, and the preserved polar vessels.

Splenic Scintigraphy

For scintigraphic examination, an activity of 0.05 mCi (1.85 MBq)/kg body weight (99-technetium zinc colloid, Albures) was intravenously injected. Depending on age and body weight, this is equivalent to an effective dose of 1.3 to 1.8 mSv. After 30 minutes, the patient was placed in a supine position and ventral and dorsal whole-body scintigraphies were taken followed by a single photon emission computed tomography scan. Then, dorsal and ventral scans taken of the region of interest (ROI) were analyzed semiquantitatively. Splenic uptake was defined as the ratio of the geometric mean of the ROI to whole-body activity. In this way, we were able to determine the percentage of radionuclide that was phagocytized by the remnant spleen. This parameter was used to test for preserved clearance function of the remnant spleen.

Pitting Activity and Thrombocytosis

Differential interference contrast microscopy was used to obtain 3-dimensional erythrocyte imaging of the surface membrane, which exhibits craters and pits in patients with total splenectomy. If splenic function is preserved completely, the percentage of pitted cells should be less than 2%. In asplenia, the percentage of pitted cells in the blood smear is elevated by up to 50%. The pitted erythrocyte count was determined on red cells from fresh venous blood fixed with 3% glutaraldehyde buffered to pH 7.4 and examined as a wet preparation using an interference-phase microscope fitted with Nomarski optics.[13]

Platelet counts were taken in EDTA blood to determine if the patients developed any thrombocytosis.

RESULTS

Patient Characteristics

The patient characteristics are detailed in Table 2. Before surgery, 62% of the 42 patients had gallstones, 73% of whom had suffered gallstone symptoms. Twenty-nine required repeated transfusions for pronounced anemia, chiefly during hemolytic crises.

TABLE 2. Demographic Data of Patients at Time of Near-Total Splenectomy

Age (yr): mean (range)	9.5 (2–42)
Sex (no.)	
Male	22
Female	20
Height (cm): mean (range)	137 (104–185)
Body weight (kg): mean (range)	32 (17.6–79)
Cholecystolithiasis (no.) (percentage)	26 (62%)
Transfusions (no.) (percentage)	29 (69%)
Patients (no.)	42

Surgical Procedure

A remnant spleen of 8 to 11 cm^3 in size could be preserved in all 42 cases. The weight of the resected spleen varied between 160 and 1510 g (mean, 580 g). The extent of resection averaged 98% (93–99%) and was thus directly proportional to preoperative spleen size. Vascular dissection was extremely difficult in 8 patients (19%) because the arteries branched very close to the hilus, ran directly along the capsule, or separated into several pairs of vessels in the region of the pole. Our method required that, whenever present, supernumerary spleens were to be extirpated completely. A total of 4 accessory spleens had to be removed. One small, solitary supernumerary spleen was removed in 2 patients and 2 supernumerary spleens were removed in 1 patient. None of the accessory spleens removed was larger than 1 cm in diameter. The locations were the omental bursa, gastrocolic ligament, gastrosplenic ligament, and greater omentum, respectively.

Whenever sonography detected gallstones, which was the case in 26 of 42 patients, and regardless of the symptomatology, we performed cholecystectomy (n = 24) or cholecystotomy (n = 2) accessing the gallbladder from the left side. Blood loss resulting from intraoperative bleeding was less than 20 mL in all operations. The mean surgery time was 65 minutes without any gallbladder intervention and 88 minutes with cholecystectomy or cholecystotomy. The first 10 operations took an average of 15 minutes longer.

The mean postoperative stay was 4.3 days. Two patients (2 and 3 years old) were transferred to the pediatric intensive-care unit for postoperative monitoring for a maximum of 24 hours. In 2 patients, resumption of a normal diet was delayed by 24 hours as a result of a gastric-emptying disorder. No relevant perioperative hemorrhagic or infectious complications were associated with this procedure. No blood transfusions were required intra- or postoperatively.

A surgical complication occurred in 1 patient who underwent 1 of the first operations performed using this technique. Back in 1996, when we performed 1 of the first NTS for this study, monopolar diathermy was used for parenchymal resection. In 1 instance, the preserved pair of vessels at the caudal pole of the spleen experienced a thermal

lesion resulting in necrosis of the residual spleen. As a result of this incident, we stopped using diathermy and only used scalpels for all later operations. In the other 41 patients, the operation was carried out successfully. In 2 of 42 cases, a drain was necessary because of bleeding from the pancreatic tail that had to be sutured over. There was no incidence of pancreatitis. At discharge, 41 patients had normal perfusion of the remnant spleen as documented by Doppler color flow.

Follow-up

Patient follow-up encompassed a period of 6 months to 6 years (mean, 3.0 years); 22 of 42 patients received 1 follow-up examination in the period between October 2002 and May 2003. Twenty of the 42 patients were lost to follow up. The reasons for this included change of residence or attending physician, refusal to return for a follow-up examination as a result of costs, and/or a too-long distance to travel to the study center. No cases of infection-related hemolysis requiring transfusion or newly formed gallstones were observed at mean follow-up.

Regrowth of the Splenic Remnant

Remnant spleen size measured by sonography was within a range of 10–56 cm^3 (mean, 32 cm^3) in the first postoperative year and 31–87 cm^3 (mean, 69 cm^3) in the second postoperative year. The rate of splenic growth was the most rapid during the first 2 post-NTS years but then slowed (Fig. 2). At follow up, Doppler color flow of the splenic vasculature showed normal blood flow in 21 of 22 patients.

One 4-year-old girl's surgery posed difficulties as a result of her vascular anatomy. At discharge her Doppler color flow was normal, but 8 weeks after surgery, the girl presented again because of left epigastric pain. Necrosis of the spleen was detected by sonography. It emerged that the parents had discontinued her acetylsalicylic acid therapy 2 weeks after discharge. A splenectomy was not deemed necessary.

None of the patients experienced any intra- or retroperitoneal sonographically detectable late complications or any new postoperative cholecystopathic disorders. There was no case of infection-related anemia or hematologic crises requiring transfusion.

Remnant Function

A spleen scintigraphy with 99-technicium was carried out on all 22 patients, with 21 showing radionuclide uptake in the left epigastric region. This positive uptake demonstrated the preservation of phagocytic activity of the remnant spleen (Fig. 3); in 76%, positive uptake was >2%. There was no correlation between the amount of uptake and length of follow-up.

In 2 patients, the pitted red cells were <2%, in 3 patients between 20% and 26.3%, ranging between 2% and 20% in the rest (n = 16). Thus, the elevated values showed a reduced but still existent splenic phagocytotic activity (Fig. 4). Platelet counts tended to drop slightly within 3 to 6 months and remained above the normal range, but without requiring therapy, within the first postoperative year (Fig. 5).

DISCUSSION

The 2 most serious complications secondary to splenectomy are a higher rate of bacterial infection and postsplenectomy sepsis, called overwhelming postsplenectomy infection syndrome (OPSI), which develops in approximately 1% to 2.4% of splenectomy patients.[3,5] In historical retrospective

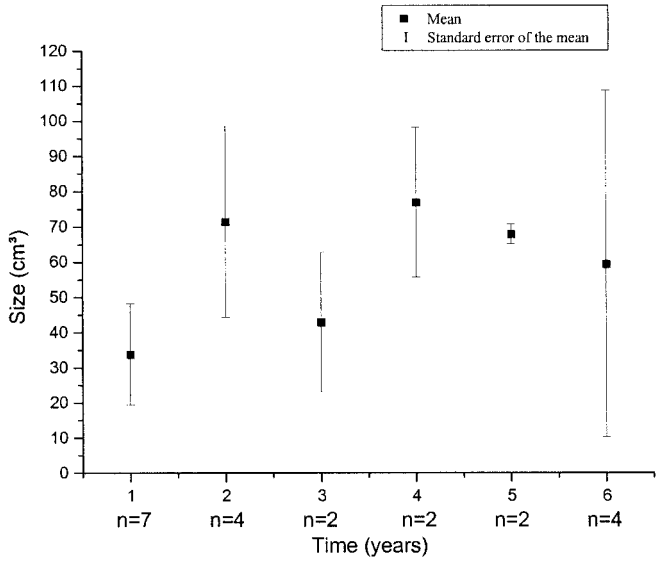

FIGURE 2. Sonographic size of the remnant spleen at follow up.

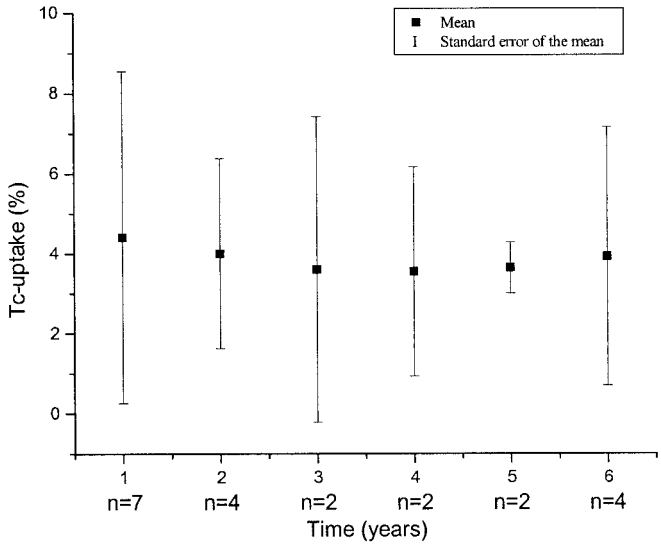

FIGURE 3. TC uptake in the remnant spleen at follow up.

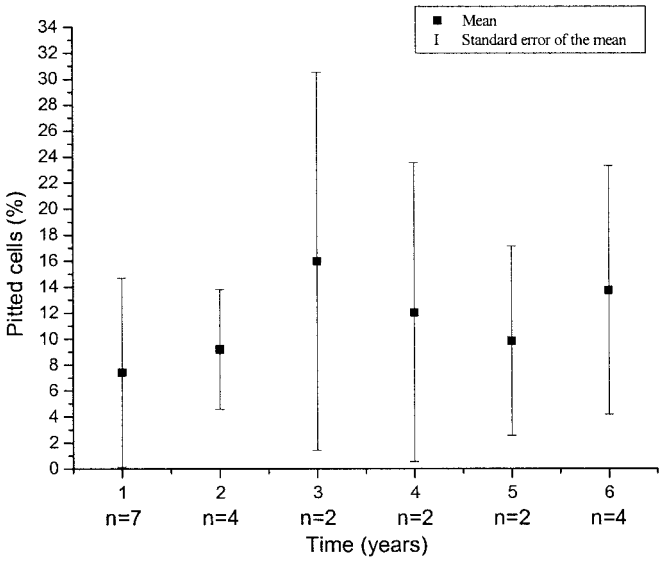

FIGURE 4. Pitting activity at follow up.

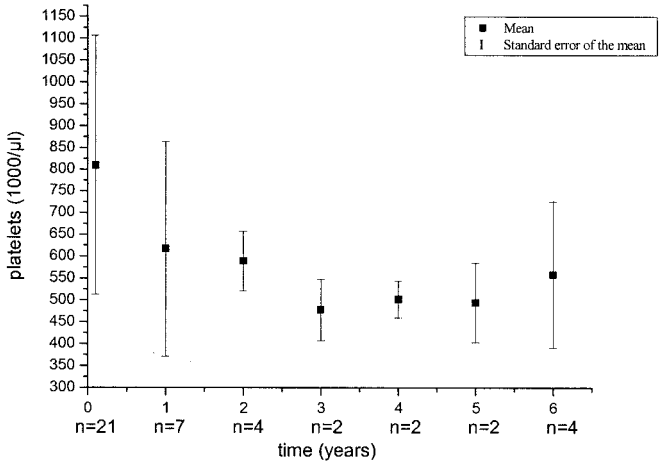

FIGURE 5. Platelet count at follow up.

studies, the majority of inhomogeneous patient samples had received insufficient vaccination protection.[5,7] OPSI is life-threatening, with a fatal outcome occurring in 45% to 75%.[3,4] In 1 study conducted by the authors on 165 splenectomized relatives of children with hemolytic anemia from 1989–1995, 4 patients (2.4%) developed postsplenectomy sepsis or meningitis between the ages of 24 and 46 years. Three patients (1.8%) who had undergone splenectomy in childhood died of an infectious complication 16 to 28 years later.[3] Schilling observed exactly the same 1.8% mortality rate 18 to 30 years after total splenectomy.[4]

Severe infections originate primarily from insufficient clearance function after total splenectomy, eg, of encapsulated bacteria and parasites in the bloodstream.[20,21] In addition, humoral immunity is significantly weakened because splenectomy results in a loss of rapid production of specific antibodies to T-cell-independent polysaccharide antigens (pneumococci, meningococci, and *H. influenzae* type B). This infectious risk, which—particularly in children and teenagers—can be increased 100-fold compared with the age-matched normal population, persists throughout life.[23] Unfortunately, vaccinations and long-term oral antibiotic prophylaxis do not offer complete protection.[24–26] Finally, the risk for thromboembolic complications and atherosclerotic lesions[9] is also increased in patients with HS and total splenectomy.

The evidence on the potential complications in splenectomized patients speaks in favor of spleen-conserving surgical techniques. We therefore intentionally chose to forego the minimally invasive procedure associated with complete splenectomy. As has been shown in laparoscopic colon surgery, there are no differences in terms of quality of life between the open and laparoscopic approaches.[27] Previous studies have already demonstrated the beneficial effects by partial or subtotal splenectomy on hemolysis, erythropoiesis, and general well-being to be gained.[1,14–19]

Indeed, the clinical course after NTS is considerably different from that after partial or subtotal splenectomy. In our cohort with an up to 6-year follow-up period (mean, 3.0 years), no patients experienced a hemolytic relapse requiring transfusion or required secondary surgery. This contrasts with the results of the subtotal technique study in which 5 of 40 patients (12.5%) required transfusions for hemolytic relapse and 3 required total splenectomy secondary to subtotal splenectomy during their 3.5-year follow up.[1] We also did not observe any infection-related hemolytic crises or thromboses. In our study, we similarly had 1 patient who developed secondary splenic necrosis 8 weeks postsplenectomy, ie, a 4.5% necrosis rate.

The largest, age-adjusted spleen volumes measured after NTS were 86 cm^3 in a 7-year-old boy weighing 29 kg 2 years postoperatively and 131 cm^3 in a 16-year-old girl weighing 51 kg 6 years after surgery. These 2 maximum volumes are thus less than the age-equivalent spleen size of a normal healthy person (4% of body weight) and very markedly below those reported by other studies.[1,14–17,19] Smaller spleen size, however, appears to be accompanied by an existing but somewhat reduced phagocytic activity.

Over a period of 7 to 56 months, new postoperative occurrences of newly formed gallstones have been observed in up to 22% of noncholecystectomized patients (4 of 18) with subtotal splenectomy.[1] One of the reasons may be the considerably large, nonstandardized size of the preserved residual spleen and the persistent hemolysis resulting from it. In this aspect, our cohort is distinguished from other studies in that not a single noncholecystectomized patient developed gallstones after surgery within the up to 6-year follow-up period. Although we observed no cases of recurrent hemoly-

sis, a lifelong risk for developing recurrent hemolysis potentially remains. No longer-term data are currently available.

Optimum blood flow, however, is also crucial for maximum perfusion of all 3 functional zones of the remnant and consistently high rate of venous return through the large-caliber splenic vein and for preventing portal vein thrombosis. These functional requirements justify the need to preserve the blood flow of the residual spleen through the hilar, not through the short gastric vessels. The effects of blood flow on cardiac output, immunologic stimuli, and innervation of the remnant have also been discussed as contributing factors.[12]

Posttotal splenectomy immunodeficiency, loss of clearance function, insufficient vaccination protection, and antibiotics and vascular risks are all additional factors that speak in favor of preserving some portion of the spleen.

Compared with other spleen-preserving procedures, our patients only showed moderate splenic growth with no recurrence of HS. There was no inversely proportional correlation between residual spleen size and pitting activity during follow up, and there was not a proportional relationship between remnant volume and TC uptake. These observations were unexpected after NTS and cannot currently be explained. The number of pitted cells is a rough measurement and may not reflect the true extent of phagocytosis.

The post-NTS residual spleen shows a high long-term survival rate with demonstrable technetium uptake, indicating preservation of phagocytosis. The intact clearance function post-NTS provides better protection in the early phase of bacteriemia that after total splenectomy. However, the minimal, immunologic, and phagocytotically still effective spleen size, or "minimal critical mass," has not been sufficiently delineated.

In terms of the frequency of recurrent hemolysis and repeat surgery, NTS would seem superior to partial and subtotal splenectomy. Additional results of ongoing studies on immunologic function in this syndrome will be presented soon. Given the lifelong increased risk of severe infection and the thromboembolic risk potential in patients living without a spleen, the medical, ethical, and legal justification for total splenectomy, especially in children, should be critically reappraised as the interventional modality of choice for moderate to severe forms in hereditary spherocytosis. Spleen-preserving resection should be considered as first-line therapy because of the especially high risk of fatal sepsis in children splenectomized before the age of 5 years and the lifelong risk of overwhelming postsplenectomy infection syndrome (OPSI). Exhaustive investigation of the immunologic function remaining after partial, subtotal, and near-total splenectomy is required to further elucidate the risks of recurrent hemolysis and to define "minimal critical mass" of the residual spleen.

NTS is a safe and effective technique for the management of hereditary spherocytosis with a low intra- and postoperative complication rate, specifically with regard to bleeding, that poses no higher risk than total splenectomy. Based on clinical outcome, NTS appears to provide more long-term benefits.

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