Splenectomy is the most common surgical procedure in patients with hematological disorders. In many hematological conditions, the physiological and pathological (hypersplenism) function of the spleen is regulated by the occurrence of numerous clinical symptoms. As a result, the removal of the above-mentioned organ should eliminate the basic chain link of the pathogenetic process. However, in some patients, splenectomy does not promote regression of clinical symptoms. Thus, the basic problem in splenic surgery is associated with the absence of indices, which would predict the distant effects of splenectomy.

The aim of this study was to retrospectively determine the indications for splenectomy and its efficacy in adult patients with hematological disorders, as well as the influence of certain objective factors on the therapeutic effect of splenectomy.
MATERIAL AND METHODS

The study group was comprised of 98 adult patients subjected to splenectomy, due to many hematological disorders during the period between 1994 and 2004, at the 2nd Department of General and Oncological Surgery, Medical University in Wroclaw. The study group was comprised of 53 (54.1%) patients with idiopathic thrombocytopenic purpura (ITP), 25 (25.5%) with malignant lymphomas, 9 (9.2%) with hereditary spherocytosis, six (6.1%) with acquired hemolytic anemia, and two (2%) with myelofibrosis (tab. 1). The mean duration of treatment was 12.5 days.

Analysis of the disease course was based on medical documentation obtained from the 2nd Department of General and Oncological Surgery, Medical Academy in Wroclaw, Department of Hematology, Medical Academy in Wroclaw and Hematological Outpatient Clinic, SPSK Hospital in Wroclaw, as well as questionnaires completed by the patients.

The disease was divided into the preoperative, operative and postoperative periods. The preoperative period was comprised of information concerning the duration of the disease, main symptoms and course, laboratory parameters, and conservative treatment applied with subsequent therapeutic effect prior to surgical intervention. Splenomegaly was based on the Walas classification (1), which distinguished mild splenomegaly (spleen was palpable below the left costal arch), from moderate (the lower pole of the spleen was at the level of the umbilicus), and significant splenomegaly (spleen crossed-over to the right side of the abdomen). In the perioperative period, the following were considered: indications for splenectomy, type of surgical intervention, patient preparation, duration of hospitalization, perioperative blood transfusions, early complications and variability of selected laboratory parameters (tab. 2).

Table 1. Gender and average age of patients subjected to splenectomy, due to hematological disorders

<table>
<thead>
<tr>
<th>Hematological disorders</th>
<th>Average age</th>
<th>Gender (female: male ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic thrombocytopenic purpura</td>
<td>35.9</td>
<td>43 : 10</td>
</tr>
<tr>
<td>Hereditary spherocytosis</td>
<td>29</td>
<td>2 : 7</td>
</tr>
<tr>
<td>Acquired hemolytic anemia</td>
<td>34</td>
<td>2 : 1</td>
</tr>
<tr>
<td>Malignant lymphomas</td>
<td>49</td>
<td>11 : 14</td>
</tr>
<tr>
<td>Leukemia</td>
<td>45.7</td>
<td>2 : 4</td>
</tr>
<tr>
<td>Myelofibrosis</td>
<td>47</td>
<td>2 : 0</td>
</tr>
</tbody>
</table>

Table 2. Indications for splenectomy considering patients with hematological disorders

<table>
<thead>
<tr>
<th>Hematological conditions</th>
<th>Indications to perform splenectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic thrombocytopenic purpura (ITP)</td>
<td>– treatment of “disease remission” resistant to pharmacological therapy</td>
</tr>
<tr>
<td>Acquired immunohemolytic anemia (AIHA)</td>
<td>– frequent disease exacerbations (hemolytic crisis) requiring intensive, long-lasting blood transfusions,</td>
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<tr>
<td></td>
<td>– presence of warm type antibodies,</td>
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<td></td>
<td>– ineffective pharmacological therapy</td>
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<tr>
<td>Hereditary spherocytosis</td>
<td>– medium and severe form of the disease,</td>
</tr>
<tr>
<td></td>
<td>– frequent disease exacerbations (hemolytic crisis) requiring intensive, chronic blood transfusions,</td>
</tr>
<tr>
<td></td>
<td>– spherocytosis complications, especially presence of cholelithias</td>
</tr>
<tr>
<td>Malignant lymphomas</td>
<td>– significant splenomegaly,</td>
</tr>
<tr>
<td></td>
<td>– hypersplenism symptoms: mono-, bi- or pancytopenia,</td>
</tr>
<tr>
<td></td>
<td>– splenic localization of the disease,</td>
</tr>
<tr>
<td></td>
<td>– lack of therapeutic effect following chemotherapy in case of hairy cell leukemia (treatment of remission)</td>
</tr>
<tr>
<td>Leukemia</td>
<td>– posttraumatic or idiopathic rupture of the spleen,</td>
</tr>
<tr>
<td></td>
<td>– significant splenomegaly</td>
</tr>
<tr>
<td>Myelofibrosis</td>
<td>– significant splenomegaly</td>
</tr>
<tr>
<td></td>
<td>– hypersplenism symptoms: mono-, bi- or pancytopenia,</td>
</tr>
<tr>
<td></td>
<td>– symptoms associated with splenomegaly (abdominal pain)</td>
</tr>
</tbody>
</table>
All patients were subjected to classical splenectomy. Thus, we eliminated the influence of the type of surgical technique.

The observation of results following splenectomy enabled us to distinguish patients who benefited from the procedure, as well as those, where splenectomy proved ineffective. The final effect following splenectomy was determined one month after the operation. Considering the type of hematological disorder, patients were divided into six groups. We were able to determine mutual correlations between surgical treatment results, and selected clinical and laboratory parameters, as well as present group patient characteristics. The analysis of the above-mentioned was based on the Pearson’s test, and in case of a small number of observations (<25) – Fisher’s test. p<0.05 was considered as statistically significant.

RESULTS

During the period between 1994 and 2004, 98 splenectomies were performed at the 2nd Department of General and Oncological Surgery, Medical University in Wrocław, due to hematological disorders, which comprised 78% of all spleen removal operations (fig. 1). Female patients predominated (63.3%). The average age of patients who qualified for splenectomy was 40.1 years. Patients with benign hematological disorders were younger relative to those with malignant diseases (33 vs 47.2 years). The number of splenectomies increased by 50% during the last five years: from 5-8 to 12-14 per year (fig. 2). The frequency of splenectomy, due to particular hematologic indications, also changed. Idiopathic thrombocytopenic purpura was the most common hematological indication for splenectomy (50-60% of all splenectomies, due to hematological disorders), and the percentage of the above-mentioned procedure remained constant over the past 11 years (fig. 3). Eight of nine procedures for hereditary spherocytosis were performed during the period between 1994 and 1999. Most splenectomies were planned (96 procedures).

The size of the removed spleen differed (fig. 3). In most patients with ITP (92.5%), the spleen was of normal size or slightly descended below the left costal arch. In case of patients with other hematological disorders, the spleen was often enormous and nearly filled the entire abdominal cavity (100% of patients with myelofibrosis, 52% with malignant lymphomas and 50% with leukemia – chronic myeloid leukemia). Moderate-sized spleens were primarily observed in patients with hereditary spherocytosis (55% of patients) and acquired hemolytic anemia (66% of patients). An accessory spleen was observed and removed in eight patients. One patient was diagnosed with two accessory spleens.

Early complications following splenectomy consisted of disturbances, which appeared during hospitalization including perioperative mortality. The above-mentioned were observed in 11 (11.3%) patients: one with acquired hemolytic anemia, two with leukemia, three with malignant lymphomas, four with ITP, and one with hereditary spherocytosis. Early complications were not observed in case of patients with myelofibrosis. During hospitalization two patients were diagnosed with deep venous thrombosis, two with pneumonia, one with pleuritis, and one with atrial fibrillation. The above-mentioned regressed following appropriate conservative therapy. Two
patients required relaparotomy, due to symptoms of internal bleeding. The perioperative mortality was 2% (2 patients). Both patients underwent emergency surgery due to rupture of the spleen during the course of leukemia.

Distant complications were analyzed in the 96 patients who survived the perioperative period. The above-mentioned complications were observed in 24 patients, which comprised 25% of all operated patients who survived the perioperative period: one patient with acquired hemolytic anemia, 4 with malignant lymphomas, 17 with ITP, one with hereditary spherocytosis and one with myelofibrosis. The following should also be considered: venous thrombosis of the lower limbs (3 patients), upper extremity venous thrombosis (one patient), portal thrombosis (one patient), frequent upper respiratory infections (11 patients), pneumonia (two patients), intugement infections (one patient), postoperative scar hernia presence (one patient), as well as intestinal obstruction treated by means of conservative therapy. Two ITP patients were diagnosed with symptom recurrence after an initial favorable effect following splenectomy (after 20 and 84 months), while one patient presented with autoimmunological hematological disturbances (Evans syndrome). Severe sepsis was not observed after splenectomy (overwhelming post-splenectomy infection).

Splenectomy proved beneficial in 41 patients with ITP (77.4%): in 31 patients we observed an increased platelet count (>100x10^9/l); thrombocytopenic symptoms were absent in six patients, in spite of platelet counts ranging between 50-99x10^9/l. Satisfactory surgical treatment results were also observed in the setting of a 50% corticosteroid dose reduction prior to splenectomy or with cyclic administration in four subjects with thrombocytopenia immediately after the procedure. As a consequence of pharmacological therapy, the course of the disease was mild. Disease recurrence was observed in two patients.

Statistically significant differences (p<0.05) were noted between ITP patients with satisfactory and non-satisfactory splenectomy effects, considering the following factors: time from diagnosis to splenectomy (54.4 months vs. 25.3 months), mean and lowest platelet count before the procedure (68 and 54x10^9/l vs. 36 and 23x10^9/l, respectively), value of the spleen-liver index (SLI>1 in 9 of 11 patients with a satisfactory splenectomy effect vs 2 of 6 with a non-satisfactory effect), variability in the platelet count after splenectomy (exceeding 100x10^9/l one day after the procedure and 400x10^9/l seven days after satisfactory splenectomy) (fig. 4, 5 and 6).

The beneficial effect of splenectomy in eight (88.9%) patients with hereditary spherocytosis was manifested by decreased hemolysis (conjugated bilirubin <1 g%, percentage of reticulocytes <3% and regression of jaundice), and normalization of morphological values (hemoglobin level >12 g%, hematocrit > 40% and number of erythrocytes >3x10^12/l). The above-mentioned patients required no conservative treatment, nor blood transfusions. Splenectomy did not improve the clinical course of the disease in only one (11.1%) female patient. He-

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Fig. 3. Splenomegaly in patients subjected to splenectomy, due to hematological disorders

moglobin values remained low (<6 g%) with episodes of syncope, and she required blood transfusions.

The positive effect of splenectomy was considered in acquired hemolytic anemia patients when morphological parameters normalized, and symptoms of hemolysis regressed (similarly to hereditary spherocytosis) without the need for conservative therapy. This was the case in two of three operated patients. All above-mentioned patients were diagnosed with the presence of warm anti-erythrocytic antibodies.

Considering patients with malignant lymphomas, splenectomy improved the clinical condition (regression of cytopenia symptoms, reduction of pain, and slowed course of the disease) in 18 (72%) subjects. However, splenectomy proved non-beneficial in seven patients. These patients presented with disease progression and hematological disturbances remained constant.

Significant differences (p<0.05) were observed in patients with satisfactory and non-satisfactory splenectomy effects with respect to
the following factors: number of leucocytes before the procedure (leucocytosis or normal values in 14 of 19 patients with satisfactory splenectomy effects vs. 2 of 6 patients with non-satisfactory splenectomy effects), and histopathological diagnosis (satisfactory splenectomy effect was observed in 12 of 14 patients with non-Hodgkin’s lymphomas and 6 of 11 patients with Hodgkin’s lymphomas) (fig. 7).

In patients with myelofibrosis, splenectomy was of palliative character resulting in amelioration of the most severe symptoms associated with splenomegaly and hypersplenism. In one female patient, splenectomy lead to the regression of abdominal cavity symptoms, while one patient remained with significant anemia symptoms, which proved that the beneficial effect of splenectomy was not attained. Removal of the spleen did not promote disease stabilization in both subjects.

All splenectomies in patients with leukemia were emergency procedures, due to rupture of an enlarged spleen (three patients) or planned procedures in case of significant splenomegaly, in order to avoid spontaneous rupture (three patients). Thus, splenectomy proved beneficial, although had no influence on disease course.

**DISCUSSION**

Splenectomy is an important procedure in the management of numerous hematological disorders. Data analysis demonstrated several epidemiological changes, which occurred during the past ten years, with respect to patient qualification for splenectomy. During the period between 1994 and 2004, the number of splenectomies performed to treat hematological disorders significantly increased. During the period between 1994 and 1998, five to eight such procedures were performed, while in the subsequent five years 12 to 14 splenectomies per year were performed. Due to inflammatory prophylaxis in patients after splenectomy and the less frequent occurrence of infectious complications, the above-mentioned procedure in case of acquired hemolytic anemia is performed in children under the age of five years.

Delayed surgery is rarely observed. Idiopathic thrombocytosis is the most common hematological indication for splenectomy. Wood and co-authors obtained similar results on the basis of their five-year observation period, considering patients subjected to splenectomy, due to hematological disorders: 41% of patients were diagnosed with chronic idiopathic thrombocytosis, 10% with acquired hemolytic anemias, 9% with myeloproliferative syndromes, 13% with malignant lymphomas, 19% with acute and chronic leukemias, and 8% with other disorders. The number of splenectomies performed in patients with leukemia is surprising (2).

The size of the removed spleen varied, although a correlation was observed between the size of the spleen and the hematological disorders. In patients with idiopathic thrombocytopenic purpura, the spleen was of normal size or slightly enlarged (92.5% of patients). Thus, the majority of splenectomies were performed by laparoscopy (3, 4). However, significant splenomegaly was observed in patients with malignant lymphomas, leukemia and myelofibrosis. In patients with hereditary spherocytosis and acquired hemolytic anemia, moderate splenomegaly was observed. The above-mentioned had no prognostic significance considering the surgical procedure, but it influenced the operative technique. Patients with splenomegaly
required frequent blood transfusions relative to those with normal-sized spleens, which was confirmed by other authors (5). Accessory spleens were found in 10-20% of patients (6, 7), which proved similar to our findings.

Early and distant complications associated with splenic dysfunction were of mild character and often regressed after conservative therapy. Early complications occurred in 11.3% of patients, while distant complications occurred in 24.5%. Kojouri and co-authors (8) presented similar results in their meta-analysis and demonstrated that perioperative mortality in patients subjected to classical splenectomy was 1%, while the frequency of early complications was 12.9% (8). No statistically significant dependence between the frequency and type of postoperative complications and the effect of splenectomy was observed. Although early complications occurred more often in patients with a non-satisfactory splenectomy effect (12.5% vs 9.8%), the difference was nonsignificant. Distant complications proved similar with respect to satisfactory and non-satisfactory splenectomy patient effects (26.8% vs 23.8%).

Fifty-three (54.1% of all splenectomies connected with hematological disorders) operations were performed for chronic idiopathic thrombocytopenic purpura (ITP). Similar data were presented by colleagues from the Department of Surgery, Institute of Hematology and Transfusiology in Warsaw (9). Spontaneous regression of thrombocytopenic symptoms is rarely observed. First-line treatment, both steroid and immunosuppressive therapy, does not abolish thrombocytopenic symptoms. The lack of therapeutic effect after several months of conservative treatment is an indication for surgical intervention (10).

We observed a positive effect of surgical treatment in nearly 70% of patients with idiopathic thrombocytopenic purpura. The remission index after splenectomy in case of ITP patients ranged between 64% and 90% (11-16). In a meta-analysis, Kojouri and co-authors (135 investigations during the period between 1996 and 2004) examined the effect of splenectomy in patients with idiopathic thrombocytopenic purpura and demonstrated that the complete remission was 66% (2623 patients), while partial remission was observed in 88% of patients (8). The lack of definition concerning the criteria of complete and partial remission in patients treated for ITP rendered the comparison of data between particular authors difficult. Radaelli and co-authors considered the platelet count >100x10⁹/l (17), as evidence of complete remission, while Schwartz used 150x10⁹/l as the cutoff (14). Since some patients present with recurrence of thrombocytopenic symptoms after splenectomy, it is important to determine the time elapsed from surgical intervention to treatment evaluation.

The prevalence of platelet sequestration in patients with ITP remission after splenectomy was demonstrated by numerous authors. Some demonstrated statistical significant association between the spleen-liver index (SLI) and the effect of splenectomy (19, 20), while others demonstrated no such association (21, 22). Localizing the area of platelet destruction is of prognostic value. For cases in which splenectomy was beneficial, platelet destruction was observed in the spleen, while in case of the non-satisfactory effect, platelet destruction predominated in the liver.

Some authors confirmed the correlation between the duration of conservative therapy and the effect of splenectomy (13, 23), while others reported otherwise (11, 12, 14, 18, 23, 24). Kwon and co-authors (23) demonstrated that best splenectomy effects were obtained if pharmacological therapy lasted less than 12 months. Sikorska and co-authors (23) distinguished two optimally prognostic time intervals: <107 months and >261 months from diagnosis to surgical intervention. Based on our own results, the duration of conservative therapy prior to spleen removal was twice as long in patients with ITP and a satisfactory splenectomy effect (54.5 months vs 25.3 months). Portielje and co-authors (26) demonstrated that the decision for splenectomy should not be delayed in cases of benign hematological diseases. The above-mentioned is associated with the fact that mortality, due to severe infections attributed to chronic immunosuppressive therapy, exceeds mortality associated with massive hemorrhage after spleen removal.

An important prognostic factor in ITP was attributed to the platelet count before splenectomy and its variability during the initial ten days after the procedure. Remission of clinical symptoms was observed in benign thrombocytopenia and in patients with platelet counts exceeding 400x10⁹/l seven days after splenectomy. This was similar to data obtained by
other authors (21). There was no association between the beneficial effect of splenectomy and patient response to preoperative conservative treatment (corticosteroids, intravenous immunoglobulins).

Poor surgical treatment outcomes were observed in patients with acquired hemolytic anemia (AIHA), although our study only had three AIHA patients, which made it impossible to determine any statistical significance between analyzed parameters and the beneficial effect of splenectomy. All patients with AIHA were diagnosed with warm type antibodies. The literature also demonstrated disease course improvement in case of warm antibodies, contrary to the presence of cold antibodies (27).

Hereditary spherocytosis, one of the primary indications for splenectomy, was first described in 1871 and treated by means of splenectomy (28). Splenectomy in case of hereditary spherocytosis does not eliminate the genetic defect, but improves the course of the disease, eliminating the area for erythrocyte apoptosis. The beneficial effect of splenectomy was observed in 90% of patients in accordance with the literature (27, 28, 29).

The qualification of patients with hereditary spherocytosis for splenectomy should be based on the presence of severe clinical symptoms or accompanying complications (cholelithiasis in three patients) (30). It is estimated that gall-bladder deposits develop in 30 – 60% of patients with hereditary spherocytosis (29). Bolton-Maggs and co-authors (28) considered the family history to be helpful when deciding on surgical intervention. If splenectomy reduced hemolytic anemia symptoms in relatives of patients with hereditary spherocytosis, the above-mentioned procedure would also prove beneficial in these patients. This was confirmed in one of our study patients.

The treatment of patients with malignant lymphomas and leukemia consists of radiotherapy and/or chemotherapy. Surgical intervention usually limits splenomegaly and hypersplenism complications. Its beneficial effect on prognosis is only observed in case of splenic localization of the disease. In the remaining cases, splenectomy does not prolong life, although it improves the quality of life (31). This was the rationale for splenectomy in patients with malignant lymphomas. Indications for explorative laparotomy were considered during the early stages of the disease, limiting the surface of irradiation (32). The beneficial effect of splenectomy in patients with non-Hodgkin’s lymphomas might be associated with the presence of six patients with hairy-cell leukemia. Until recently, surgery was the treatment of choice for hairy-cell leukemia (33). However, the introduction of interferon alfa and purine analogues practically eliminated the need for splenectomy in such patients (34). Splenectomy is rarely performed in such patients, only in emergency cases or in case of severe splenomegaly complications.

Similar to other authors (35), splenectomy in patients with myelofibrosis was considered a palliative treatment used to alleviate pain. Indications for splenectomy are as follows: transfusion-dependent anemia, symptomatic splenomegaly, portal hypertension, and significant thrombocytopenia (<20x10⁹/l) (36). Some investigations demonstrated the increased risk of blastic transformation or development of pulmonary hypertension in patients with myelofibrosis after splenectomy (37, 38). One of the splenectomized patients developed blastic transformation requiring cytostatic therapy, which proved effective.

CONCLUSIONS

1. The indications for splenectomy should depend on the clinical situation. In case of hematological disorders, splenectomy should be performed when clinical “advantages” exceed the “disadvantages” associated with asplenic complications.

2. Splenectomy alleviates the clinical course of the disease in most patients with idiopathic thrombocytopenic purpura (41/53 patients), acquired hemolytic anemia (2/3 patients), and hereditary spherocytosis (8/9 patients), but it does not promote complete recovery.

3. In malignant hematological disorders with splenomegaly and/or hypersplenism, spleen removal avoids possible complications and improves the patients’ quality of life.

4. Proper patient preparation and management after splenectomy reduces the risk of postoperative complications.
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Splenectomy in patients with hematological disorders – our experience

Splenectomy is the method of choice in the treatment of numerous hematological disorders. Indications for splenectomy have changed in the past years and are associated with progress in hematological diagnostics and pharmacological therapy. Anticipation of distant results is difficult because of the absence of reliable clinical and laboratory features.

Based on the obtained results, the Authors retrospectively evaluated splenectomy indications. Idiopathic thrombocytopenic purpura proved to be the most common disease entity requiring splenectomy. The Authors obtained satisfactory splenectomy results in 77% of cases, including patients with the platelet count ranging between 50 and 99x10^9/l, as well as those with ITP treated by means of lower corticosteroid doses. These criteria require modification. Currently, complete remission is considered in patients with an increased post-splenectomy platelet count (≥100x10^9/l) evaluated around post-operative day 30. Increased platelet count exceeding ≥50x10^9/l is considered partial remission. All other cases are considered as treatment failure.

The efficacy of splenectomy in ITP was determined on the basis of results obtained 30 days after the operation. It would seem useful to compare these results with those obtained after a more distant period. The following question remains to be answered: What is the expected time of complete remission after splenectomy? Based on our results, the percentage of complete remission cases decreases with time (even up to 10%). In some patients, this is associated with the presence of accessory spleens, overlooked during the operation. The literature demonstrates a lack of correlation between complete response to splenectomy and duration of the observation period. One can observe the decreased, but non-significant, number of complete remissions.

The Authors also determined the association between selected clinical features and a favorable effect of splenectomy in ITP patients. They noted a correlation between the favorable effect of splenectomy and the duration of conservative treatment, platelet count before the operation, splenic destruction of platelets and significant variability in the platelet count between the first and seventh days after the operation. These correlations influence the expected index of complete remissions in ITP patients.

Good results were obtained in patients with hereditary spherocytosis and acquired hemolytic anemia. Splenectomy in severe cases usually leads to favorable effects, being considered as a classical indication in case of spherocytosis. The utility of splenectomy for the treatment of lymphatic system disease is unclear. Splenectomy has no influence on the prolongation of survival and often promotes the rapid progression of proliferative lesions. Thus, indications for splenectomy should be thoroughly considered. However, the decreased variability in lymphatic proliferation observed in 72% of patients is worth mentioning.

The presented study is of great practical value and is a valuable publication detailing the surgical treatment of hematological disorders.

Dr hab. med. Andrzej B. Szczepanik
Klinika Chirurgii Ogólnej i Hematologicznej
Instytut Hematologii i Transfuzjologii w Warszawie