ANALYSIS OF SELECTED CLINICAL AND LABORATORY PARAMETERS IN PATIENTS WITH SPLENECTOMY COMPLICATIONS DUE TO HEMATOLOGICAL DISORDERS

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The aim of the study was to investigate the role of certain clinical characteristics and laboratory examination results as prognostic factors for complications after splenectomy in patients with hematological disorders.

Material and methods. Ninety-eight adult patients with hematological disorders who underwent splenectomy in our department between years of 1994 and 2004. A retrospective analysis of the medical records from patients who underwent splenectomy was conducted; we divided the patients into 6 groups with various postoperative complications; patients without complications after splenectomy were the control group (the seventh group). Then, we compared patients from groups 1 – 6 with patients from the control group (group 7) before and after splenectomy with regard to various parameters including age, sex, presence of splenomegaly or accessory spleen, the operation's duration, hemoglobin level, number of erythrocytes, leukocytes and plateletes, levels of protein and fibrinogen, activity of prothrombin, INR, APTT, TT, proteinogram and levels of IgG, IgM and IgA.

Results. We found that postoperative complications, especially early complications, were more common in groups with malignant hematological complications and in older patients. Infection complications appear more often in men than in women with benign hematological disorders. The sustained platelet level elevation after splenectomy is positively associated with a higher number of thrombotic complications. Also, a lower level of gamma globulin, IgG and IgM after splenectomy correlated with a higher number of infection complications.

Conclusions. Splenectomy in patients with hematological disorders is burdened with small risks of postoperative complications. Some clinical and laboratory parameters can be used to select the group of patients with higher risks of complications, but there remains a lack of objective prognostic factors which are sure in every clinical situation.

Key words: splenectomy, hematological diseases, splenectomy complications

Indications for splenectomy in patients with hematological disorders are considered individually based on the clinical condition, course of the disease, and laboratory results. One of many criteria which should be considered when qualifying hematological patients towards splenectomy is the possible risk of early and distant complications following the procedure. Some of these complications are associated with asplenia and physiological changes which occur after splenectomy such as increased platelet count favoring thromboembolic complications. Other disturbances are connected with dysfunction of the spleen (immunity and filtration). In patients after splenectomy, one can observe complications associated with the surgical technique specific to a certain location (pancreatitis, gastric disorders, large bowel
perforation) or non-specific for the operated area (wound suppuration, intraperitoneal abscesses, mechanical obstruction, and postoperative bleeding). The general condition of many patients, especially those with malignant hematological disorders, is often severe; this additionally deteriorates prognosis, favoring the development of perioperative complications.

The aim of the study was to retrospectively analyze early and distant complications following splenectomy in patients with different hematological disorders in search of objective clinical and laboratory parameters enabling identification of patients at risk for the above-mentioned complications.

MATERIAL AND METHODS

The study group was comprised of 98 adult patients subjected to splenectomy due to different hematological disorders during the period between 1994 and 2004, at the 2nd Department of General and Oncological Surgery, Medical University in Wrocław. The study group comprised the following: 53 (54.1%) patients with idiopathic thrombocytopenic purpura (ITP), 25 (25.5%) patients with malignant lymphomas, 9 (9.2%) patients with hereditary spherocytosis, 6 (6.1%) patients with leukemia, 3 (3.1%) patients with acquired hemolytic anemia, and 2 (2%) patients with osteomyelofibrosis.

Patients subjected to splenectomy were divided into the following seven groups:
1) Patients with thromboembolic complications (venous thrombosis of the upper and lower limbs), 2) patients with infectious complications (respiratory infections, pericarditis, and dermatitis other than the operative wound), 3) patients with early surgical complications (bleeding at the site of the removed spleen), 4) patients with distant surgical complications (postoperative hernia, intestinal obstruction), 5) patients with circulatory and respiratory insufficiency and ensuing death, 6) patients with other complications after splenectomy (Evans syndrome, atrial fibrillation), and 7) patients without early and distant complications after splenectomy – the control group.

Considering the above-mentioned groups we additionally distinguished subgroups with benign hematological disorders (idiopathic thrombocytopenic purpura, hereditary spherocytosis, acquired hemolytic anemia) and malignant hematological disorders (malignant lymphomas, leukemia, osteomyelofibrosis). Afterwards, we compared the following clinical factors between every group and control patients: age, gender, presence of splenomegaly, duration of the procedure, eventual accessory spleens, as well as selected hematological parameters (hemoglobin level, erythrocyte, leucocyte and platelet counts). These were measured prior to the procedure and one day after the procedure, as well as seven days and one year following the procedure. Additionally, biochemical parameters (protein and fibrinogen levels, prothrombin activity, INR, APTT, TT) were evaluated before and after the procedure, separately for patients with benign and malignant hematological disorders.

In the case of group 2 patients, we additionally compared to control values a proteinogram and IgG, IgM and IgA levels before and after the procedure. The classical chi² Pearson test was used during analysis, and in case of a small number of observations (<25) the non-parametric, specific Fisher’s test was used. p<0.05 was considered as statistically significant.

RESULTS

Early complications after splenectomy were considered when the complication was diagnosed during patient hospitalization; this includes perioperative mortality. The above-mentioned occurred in 11 (11.3%) patients: 6 (9.2%) with benign and 5 (15.1%) with malignant hematological disorders (tab. 1). Perioperative mortality amounted to 2% – two patients subjected to emergency splenectomy due splenic rupture during the course of leukemia. Distant complications were evaluated in 96 patients who survived the perioperative period. Distant complications developed within one to 84 months after splenectomy in 21 subjects; this amounted for 21.8% of all operated patients which survived the perioperative period (16-24.6% patients with benign, and 5-16.1% with malignant hematological disorders) (tab. 2). Early complications after splenectomy occurred more often in patients with malignant disorders in comparison to those with benign hematological diseases, however the reverse is true for distant complications. These differences were statistically insignificant. All patients that developed complications were older than control subjects, with exception of two: one was diagnosed with postoperative hernia (24 vs 34.6
years in the control group), and one patient with leukemia was diagnosed with postoperative bleeding (32 vs 47.8 years in the control group) (fig. 1). The differences considering patient age were statistically insignificant. Based on the gathered data, male subjects with benign hematological disorders were more often diagnosed with respiratory tract infections in comparison to female patients (7 women: 5 men vs 37 women: 12 men). The difference was statistically insignificant (tab. 3).

The presence of accessory spleens did not correlate with the development of complications after splenectomy. However, splenomegaly in patients with hematological disturbances significantly hindered removal of the spleen, increasing the risk of early complications. Thus, the duration of the procedure in cases of postoperative peritoneal bleeding was longer in comparison to the control group (155 min vs 112 min in cases of benign hematological disorders, and 175 min vs 138 min in cases of malignant hematological disorders), as well as circulatory and respiratory insufficiency (190 min vs. 138 min). The above-mentioned differences were statistically significant. Additionally, the duration of splenectomy was longer in patients with postoperative hernia (130 min vs. 112 min). The difference was statistically insignificant (tab. 3 and fig. 2).

Table 1. Early complications after splenectomy due to hematological disorders

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Number of complications in splenectomized patients with</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HS</td>
<td>ITP</td>
</tr>
<tr>
<td>Deep venous thrombosis of the lower limbs</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Exsudative pericarditis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Internal bleeding (re-laparotomy)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Circulatory et respiratory insufficiency (death)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
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<td>4</td>
</tr>
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</table>


Table 2. Late complications after splenectomy due to hematological disorders

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Number of complications in splenectomized patients with</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HS</td>
<td>ITP</td>
</tr>
<tr>
<td>Recurrent upper respiratory tract infections</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Venous thrombosis of the limbs</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Brachial vein inflammation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Zakrzepica żyły wrotniej / portal vein thrombosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Postoperative hernia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chronic purulent dermatitis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Autoimmune hemolytic anemia (Evans syndrome)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>14</td>
</tr>
</tbody>
</table>

Interpretation of abbreviations vide tab. 1

Fig. 1. Patients’ age due to hematological disorders with development of postoperative complications (groups 1-6), and without complications (group 7)
Considering the analyzed laboratory parameters, both in cases of benign and malignant hematological disorders with thromboembolic complications, the platelet count was significantly increased seven days (542 and 494 vs 443 and 388) and one year (567 and 755 vs 378 and 402) after the procedure, in comparison to the control group.

Decreased protein levels were observed prior to and after the procedure in patients who died during the perioperative period subjected to emergency operations (4.9 g/l and 3.9 g/l vs 6.5 g/l and 5.8 g/l in case of the control group), as well as in patients who developed late surgical complications (5.2 g/l and 4.5 g/l vs 6.8 g/l and 6.2 g/l in case of the control group). These differences were statistically insignificant.

Considering patients with both benign and malignant hematological disorders who were diagnosed with infectious complications after splenectomy, the concentrations of gamma globulin and IgG were reduced in comparison to the control group (9.7% and 829 mg% respectively, in cases of benign diseases, and 11.9% and 744 mg%, respectively, in cases of malignant hematological disorders). The level of IgM was below limits (44 mg% in cases of benign disorders, and 42 mg% in cases of malignant hematological disorders).

Coagulation parameter changes (fibrinogen level, prothrombin activity, INR, APTT, TT) were observed in two patients subjected to emergency surgery due to spleen rupture. Coagulation disturbances occurred directly before or during the development of thromboembolic complications.

**DISCUSSION**

The risk of complications after splenectomy is one of many factors analyzed when qualifying patients with hematological disorders towards the abovementioned procedure.

Early complications in the analyzed group occurred in 11.3% of patients. Perioperative mortality amounted to 2% in patients subjected to emergency procedures due to rupture of the spleen. Kojouri and co-authors presented similar results demonstrating that perioperative mortality in cases of patients subjected to classical splenectomy amounted to 1%, and early complications occurred in 12.9% of patients (1).

Distant complications following splenectomy are usually connected with impaired immunity mechanisms manifested by an increased incidence of infections in comparison to the general population (2). Sepsis is the most severe complication after splenectomy (overwhelming post-splenectomy infection – OPSI) (3, 4).
Complications that developed after hospital discharge were considered as distant. Benign recurrent upper respiratory tract infections were most common (11 patients). Significant thrombotic and infectious complications connected with splenic immunity and filtration dysfunction (pneumonia, chronic purulent dermatitis, venous thrombosis, portal vein thrombosis) were rarely observed. Surgical complications, which are not characteristic of splenectomy patients, were also observed (intestinal obstruction, scar hernia). One patient was diagnosed with Evans syndrome; post-splenectomy sepsis was not observed. Similar results were presented by other authors. Pugliese and co-authors demonstrated no cases of sepsis after 107 splenectomies during the period between 1998 and 2004 (5). Kumar and co-authors noted one case of OPSI in 140 patients subjected to splenectomy due to idiopathic thrombocytopenic purpura (6). This probably is a consequence of routine infection prophylaxis performed before and after splenectomy.

There were no statistically significant dependencies between hematological disorders and frequency or type of postoperative complication. According to Tafferi and co-authors (7), splenectomy in patients with osteomyelofibrosis was connected with the highest number of complications (31%) and significant perioperative mortality (9%). The mean survival period after splenectomy amounted to 27 months. Most common early complications were bleeding, infections, and thromboembolic disturbances. Other sources demonstrated that perioperative mortality in cases of myelofibrosis ranged between 7 and 15% (8, 9). Dutch investigators showed that the risk of pneumococcal sepsis and meningitis in children with hereditary spherocytosis after splenectomy was 284 times greater than that of the general population (10). The risk of severe infections is increased throughout the patients’ life (11, 12). In order to avoid complications connected with asplenia, some patients with hereditary spherocytosis are subjected to subtotal splenectomy (13, 14, 15). After such a procedure, apoptosis of erythrocytes is reduced with maintained function of the spleen. Further investigations are required to determine which part of the spleen should be maintained in order to reduce disease symptoms and prevent recurrence, as well as protect the patient from distant complications.

Eight patients were diagnosed with an accessory spleen, while one presented with two accessory spleens. If the accessory spleens are not removed in patients subjected to splenectomy, recurrence of symptoms is possible; this has been described by numerous authors (16, 17, 18). Data in the literature has cited the occurrence of accessory spleens in nearly 10% of patients (17, 18), which is in accordance with the abovementioned results. The presence of an accessory spleen is one of the most frequent reasons for recurrence of thrombocytopenia symptoms in patients with idiopathic thrombocytopenic purpura. Thus, such patients should be subjected to ultrasound, computer tomography, and isotope examinations in order to exclude the abovementioned reason for disease recurrence (19). During the post-splenectomy observation period none of the patients presented with a recurrence of symptoms connected with the presence of an accessory spleen. The abovementioned had no influence on the frequency of postoperative complications.

Many publications described the possibility of thrombocytosis after splenectomy (1, 20, 21). The abovementioned is connected with the removal of an organ storing 1/3 of all platelets, even up to 90% in cases of pathological conditions, and from there translocation to the blood vessels (22). During a period of two weeks one can observe a maximal increase followed by platelet count reduction. Usually the platelet count is increased (23). Based on patient observations, a long-lasting platelet count increase favors the development of thromboembolic complications. Thus, such patients should receive anti-aggregation therapy and regular follow-up. In cases of significant thrombocytosis, especially in patients with myeloproliferative disorders, thrombopheresis should be performed (23).

Some authors mention the possibility of post-splenectomy portal vein thrombosis, especially in myelofibrosis patients (7, 21). The abovementioned occurred in one of the two female patients operated upon in our department. Scharf and co-authors demonstrated that 12.8% of patients after splenectomy presented with clinically asymptomatic portal vein thrombosis, while in 1.7% of patients, symptoms were evident. Thus, the Institute of Hematology in Warsaw recommends controlled portal system flow examinations 5-7 days after splenectomy in all patients (19). Measurements of the co-
agulation system (fibrinogen level, prothrombin activity, INR, APTT and TT) during follow-up afforded no prognostic value on the occurrence of thromboembolic complications.

The spleen plays an important role in the defense reactions of the body through bacterial and foreign antigen destruction with the participation of cellular and humoral immunity mechanisms (24, 25, 26). The abovementioned occur with the participation of different immunocompetent cells which are stored and later come in contact with foreign antigens (27). Considering post-splenectomy patients with infectious complications, we observed a statistically significant reduction of IgG, IgM and gamma globulin levels in comparison to the control group; numerous publications have previously confirmed this (25, 28, 29). After splenectomy, one can observe different degrees of immunological insufficiency manifested by increased inclinations towards infection. The basic defect concerns antibody-dependent immunity connected with a decreased production of IgM (28).

Since the primary immunological response is connected with IgM, its production disturbances impair antibody-dependent immunity during the initial stages of infection (29). Admittedly, after splenectomy some functions of the spleen are taken over by the liver, lymph nodes and bone marrow. However, splenic phagocytosis is more effective, especially in the presence of low levels of foreign antibodies (30, 31). Fc fragment antibody receptors localized on the surface of splenic macrophages bind and recognize antibodies more effectively than hepatic macrophages (32). This might be connected with prolonged contact between particles.

Laparoscopic and subtotal splenectomy in patients with hematological disorders renders hope for limiting the number of post-surgical complications.

CONCLUSIONS

1. Splenectomy is a safe procedure with low risks of complication in properly prepared patients. Increased operative risk mainly concerns emergency procedures, patients with malignant hematological disorders, and the elderly.

2. Infectious complications develop more often in men with benign hematological disorders.

3. Patients with post-splenectomy thrombocytosis are more likely to develop thromboembolic complications.

4. Decreased gamma globulin, IgG and IgM values in post-splenectomy patients predispose towards the development of infectious complications, especially recurrent upper respiratory tract infections.

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COMMENTARY

Complications after splenectomy can be divided into those which occur early, typical of abdomanal operations, and those which are distant, connected with asplenia. The latter may develop many years after splenectomy.

The Authors of the study presented time criteria of both types of complications, limiting early complications to the period of hospitalization. Thus, early complications are considered if they occur during the initial 30 days after splenectomy or if they develop during a hospitalization connected with the operation. The above-mentioned is concerned with the fact that patients discharged 7-10 days after the operation often develop venous thrombosis or subdiaphragmatic abscesses. These complications are qualified as early, being directly connected with the operation. Early complications occurred in 11% of patients, which is in accordance with other data in current literature. The percentage of early complications is concerned with the basic disease requiring splenectomy, patient age, splenic weight and duration of the procedure. The Authors demonstrated no statistical dependency between these features and the percentage of complications. Our observations were ba-
Analysis of selected parameters in patients with splenectomy complications

Based on a larger patient group (450 splenectomies) demonstrating a statistically significant dependency. Thus, precise splenectomy indications should be established and performed by an experienced team of surgeons.

The Authors evaluated the dependency between the percentage of thromboembolic complications and increased platelet count after the operation, as well as between the percentage of infectious complications and decreased IgM and IgG concentrations.

Portal system thrombosis after splenectomy is considered as a life-threatening complication, due to the possibility of portal hypertension. Portal vein thrombosis observed in 1% of patients is usually asymptomatic. Patients subjected to doppler-ultrasound of the portal system before splenectomy and 7 and 30 days after the procedure were diagnosed with thrombosis in 20% of cases. Enlarged spleen, large diameter of the splenic vein and turbulent blood flow through the splenic vein are considered as risk factors. Diagnosis of portal system thrombosis is an indication towards antithrombotic therapy, and in selected cases, thrombolytic therapy.

The Authors did not administer antithrombotic treatment in cases of splenectomized patients with an increased platelet count. However, they mentioned the need for anti-aggregatory therapy and even thrombophoresis without mentioning concrete criteria. In patients with increased risk of thrombosis and increased platelet count after splenectomy (200 x 10^9/l), a prophylactic dose of LMWH is administered. In cases where the platelet count exceeds 500 x 10^9/l, patients receive half of the therapeutic of LMWH and anti-aggregatory treatment. Thrombophoresis is performed when the platelet count exceeds 1.5 x 10^{12}/l.

Infectious complications, especially of the respiratory system paired with immunological system disturbances, were observed in 12.5% of patients. None of the patients developed sepsis, which is considered fatal in 60% of cases. Antibiotic prophylaxis in infections and the use of polyvalent vaccines in all patients subjected to splenectomy significantly decreased the occurrence of complications.

The presented study is of clinical value. One is aware of the possible severe, distant complications in patients subjected to splenectomy, and thus, leads towards reflection over the need for the procedure.

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