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SPLENECTOMY FOR HAEMATOLOGICAL DISORDERS

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Abstract

Splenectomy is therapeutic for a large host of conditions. It is a consequence of expanding the list of disorders and liberalizing the indications for splenectomy in many diseases. Red blood cells disorders: autoimmune hemolytic anemia, hereditary spherocytosis, hemoglobinopathies and thalassemia are prone to splenectomy after failure of medical therapy. A variety of thrombocytopenic disorders are improved by splenectomy, and the most common indication for splenectomy is ITP (idiopathic thrombocytopenic purpura). Splenectomy is successful in reversing hypersplenism in a spectrum of disease called myeloproliferative disorders. Relief of symptoms from splenomegaly is also achieved, but it does not affect the inexorable course of the disorder. The role of splenectomy in white blood cells disorders (leukemias and lymphomas) is only palliative and facilitates chemotherapy.

Splenectomy in patients with hemathologic disorders imparts a risk of fulminant and life threatening infection "overwhelming postsplenectomy sepsis" that can be obviated by appropriate treatment.

Although splenectomy for hemathologic disorders is only therapeutic and not curative, the relief of symptoms and for some disorders facilitation of chemotherapy leads to better quality of life and longer survival.

Key words: Splenectomy, laparoscopic splenectomy, hemathologic dsorders, hereditary spherocytosis, idiopathic thrombocytopenic purpura, ITP, myeloproliferative disorders, lymphoma, overwhelming postsplenectomy sepsis.

Introduction

Galen's "organum plenum misterii", the spleen is an organ localized in left hypochodrium relative to the 9th, 10th and 11th rib. The normal length of the spleen is 7–11 cm [1]. It has many functions that can be divided in two large groups *haematologic* and *immune*. These two functions are close related to the physiology and pathophysiolgy of the spleen [2]. Splenectomy has important role in the treatment of haematological disorders, although it has only therapeutic and no curative intent the list of indications for splenectomy is expanding [3].

Indications for splenectomy in haematological disorders

Splenectomy is therapeutic for a large host of conditions. Haematological disorders can be divided into the following broad categories: red blood cell disorders and hemoglobinopathies, white blood cell disorders, platelet disorders, bone marrow disorders (myeloproliferative disorders) [2] Table 1.

Red blood cell disorders

Hereditary spherocytosis (HS) is the most common haemolytic anaemia in North Europeans. It is autosomal dominant and it results with shortened RBC life by retention and damage

of abnormal red cells, caused by an intrinsic erythrocyte membrane defect. Splenomegaly is also present [4, 5].

Table 1

Operative indications for splenectomy in haematological disorders

Disease	Splenectomy requred
Hereditary spherocytosis	Always
Hereditary eliptocytosis	Sometimes
Thalassemia	Sometimes
Sickle cell anaemia	Rarely
Autoimmune haemolytic anaemia	Usually
Autoimmune neutropenia	Sometimes
Immune thrombocytopenic purpura	Usually
Thrombotic thrombocytopenic purpura	Sometimes
Hairy cell leukaemia	Rarely
Chronic lymphocytic leukaemia	Sometimes
Chronic myelogenous leukaemia	Sometimes
Non-Hodgkin lymphoma	Sometimes
Agnogenic myeloid metaplasia	Sometimes
Mastocytosis	Rarely
Hodgkin disease	Rarely

Autoimmune Haemolytic Anaemia (AIHA) is a result of autoantibodies against antigens on red blood cells. Anaemia, splenomegaly, reticulocytosis, and elevated products of red blood cell destruction are found [6, 7].

Haemoglobinopathies: thalassemia and sickle cell disease are genetic disorders related to defect in haemoglobin synthesis. Anaemia and splenomegaly are present [8, 9, 10].

Bone marrow disorders (myeloproliferative disorders)

Characterized by an abnormal growth of early cell lines in the bone marrow. Symptomatic splenomegaly, hypersplenism early satiety, poor gastric emptying, heaviness or pain in the left upper quadrant, and even diarrhoea can be present [11, 12].

White blood cell disorders

Leukemias

Chronic Lymphocytic Leukemia (CLL) is a result progressive accumulation of long-lived but non-functional monoclonal lymphocytes. Most frequent finding is lymphadenopathy, splenomegaly and cytopenias. Hairy Cell Leukemia (HCL), characterized by splenomegaly, pancytopenia, and large numbers of abnormal lymphocytes in the bone marrow [2].

Lymphomas

Non-Hodgkin's Lymphoma (NHL) is a group of malignancies derived from the lymphoid system. A proliferation of any one of the three predominant lymph cell types – natural killer cells, T cells, or B cells – may be included in NHL. Sub-entities of NHL may be clinically classified into nodal or extranodal, splenomegaly exists in various, but not all, forms of NHL. It presents the most common primary and secondary malignancy of the spleen. Primary-splenic involvement is considered when the disease may also extend to the bone marrow (BM), peripheral blood (PB), and/or the liver, in the absence of prominent lymph node involvement [13, 14, 15].

Hodgkin's Disease (HD) is a disorder of the lymphoid system characterized by the presence of Reed-Sternberg cells. More than 90% of patients with HD present with lymphadenopathy above the diaphragm. Lymph nodes can become particularly bulky in the mediastinum, which may result in shortness of breath, cough, or obstructive pneumonia. Lymphadenopathy below the diaphragm is rare on presentation but can arise with disease progression. The spleen is often an occult site of spread, but massive splenomegaly is not common. In addition, large spleens do not necessarily signify involvement. Staging procedure for HD begins with a wedge biopsy of the liver, splenectomy, and the removal of representative nodes in the retroperitoneum, mesentery, and hepatoduodenal ligament. Staging for HD may be performed laparoscopically and it is indicated in Stage Ia-IIa patients where results may affect medical management (radiation vs chemotherapy) [2, 16, 17].

Platelet disorders

Thrombotic Thrombocytopenic Purpura (TTP) is associated with large multimers of Von Willebrand factor causing platelet clumping. Thrombocytopenia, microangiopathic haemolytic anaemia, and neurologic complications are present [2].

Idiopathic Thrombocytopenic Purpura (ITP) is a result of autoantibodies directed against platelet surface antigens. Highest incidence is in women aged 15–50. Usually idiopathic but it may be seen in conjunction with: SLE, HIV, CLL, Hodgkin's Dz, or autoimmune haemolytic anaemia. Normal platelet lifespan is de-

creased from 7–10 days to 5 hrs (or total platelet turnover 5 × normal). It may remit and relapse over time and medical treatment is successful in only about 15% of patients Splenectomy is successful in 66% of patients initially, with full response. Additional 15% with partial response, 15% of these will relapse with 1 year. Indications for Splenectomy in ITP: Persistent platelet count < 80,000/mm^3 despite therapy; Recurrence of thrombocytopenia after tapering or discontinuation of steroids; Children: indicated if there is no remission after 1 year of medical treatment [18, 19, 20, 21].

Splenomegaly and Hypersplenism

There is not a single universally accepted standard, but most would agree that an ex vivo mass of > 1 kg or a pole-to-pole length of > 15 cm generally qualifies as splenomegaly [2]. Hypersplenism on the other hand represents "Haematological effects of splenomegaly" and results in enhanced capacity of the enlarged spleen: pooling, sequestering and destroying blood cells. Thus hypersplenism is the presence of one or more cytopenias in the context of a normally functioning bone marrow. Disorders causing hypersplenism can be categorized as either (a) those in which increased destruction of abnormal blood cells occurs in an intrinsically normal spleen (e.g., hemolytic anemias) or (b) primary disorders of the spleen resulting in increased sequestration and destruction of normal blood cells (e.g., infiltrative disorders) [22, 23, 24] Table 2.

Table 2

Causes of hypersplenism in haematological disorders

Primary disease of blood cells (normal spleen)	**Primary disorder of the spleen**
Congenital	***Neoplastic***
Erythrocyte abnormality	Hairy cell leukaemia
Hereditary spherocytosis	Chronic lymphocytic leukaemia
Hereditary elyptocytosis	Chronic myelogenus leukaemia
Piruvate kinase deficiency	Non-Hodgkin lymphoma
Haemoglobin abnormality	***Cellular infiltration (haematopoesis)***
Thalessemia major	Agnogenic myeloid metaplasia
Sickle cell anaemia	Mastocytosis
Acquired	
Autoimmune haemolytic anaemia	
Autoimmune neutropenia	
Immune thrombocytopenic purpura	
Thrombotic thrombocytopenic purpura	

Why splenectomy in hypersplenism?

- Treat Splenomegaly (Compressive symptoms, risk for splenic injury if active);
- Improve blood counts – RBC's, Platelets;
- Temporize underlying condition (reduce number of required transfusions, failed medical management or facilitation of chemotherapy, pain or abcess secondary to splenic infarction.);
- Staging Procedure.

Open or laparoscopic splenectomy?

Firs recorded splenectomy dates from 1549 and was performed by Andirano Zaccarello. Traditionaly it was done by an open approach using medial or left sub costal incision. Laparoscopic splenectomy was first reported by Delaitre and Maignien in 1991 [23]. It is now accepted that laparoscopic splenectomy is safe and advantageous procedure in experienced hands that has displaced open surgery for almost all indications [25). Many studies show that laparoscopic splenectomy is indicated and safe in all benign and malignant haematological diseases [26, 27] and contraindications do not differ from that of open splenectomy [28, 29]. Contraindications include the inability to tolerate general anesthesia, uncontrollable coagulopathy, and the need for laparotomy for associated procedures. Difference is found in massive, large spleens where morbidity and conversion rates to open are higher [30, 31] but implementation of hand-assisted technique reduced them (Table 3**)**. Laparoscopic spleenctomy is also associated with shorter hospital stay in all haematological disorders. Complications related to laparoscopic splenectomy are similar to open splenectomy or other major abdominal procedures. They include intraoperative and postoperative hemorrhage; infections including wound infection, pneumonia, and overwhelming postsplenectomy sepsis (OPSS). Injury to other structures such as the colon, stomach or most notably, the pancreatic tail, which can cause pancreatic abscesses or fistulas. Other complications specifically associated with laparoscopic and open splenectomy include the risk of missed accessory spleens and portal vein thrombosis [23].

Table 3

Classification of spleens according to spleen length (spleen length is measured along strait line between two poles)

Spleen class	Spleen lenght
Normal spleen	7–11 cm
Moderate splenomegaly	12–20 cm
Massive splenomegaly	21–30 cm
Megaspleen	> 30 cm

Laparoscopic splenectomy

Most LS (laparoscopic splenectomy) procedures are now performed with the patient in the right lateral decubitus position (Figure 1 and 2). A midway "double-access" technique in which the patient is in a 45-degree right lateral decubitus position has also been advocated. The double-access technique requires the placement of five or six trocars. The lateral approach routinely involves the use of three or four trocars. Use of an angled (30- or 45-degree) laparoscope (2 mm, 5 mm, or 10 mm) greatly facilitates the procedure. Exposure of the vital anatomy in a manner that allows for a more intuitive sequence of dissection, paralleling that of OS, may be considered an additional advantage of the lateral approach (Figure 3). Placement of trocars in the left upper quadrant should be performed under laparoscopic visualization, particularly if any degree of splenomegaly exists, because the latter can significantly reduce the available operating space. As with OS, the splenocolic ligament and the lateral peritoneal attachments are divided with resultant medial mobilization of the spleen. The short gastric vessels may be divided by any number of methods, including individual application of clips, endovascular stapling, or, most commonly, use of hemostatic energy sources as in ultrasonic dissection, diathermy or bipolar compression coagulation. With the lower pole of the spleen gently retracted, the splenic hilum is accessible to further applications of clips or an endovascular stapling device. The splenic artery and vein are divided separately when possible. Good long-term outcomes, however, are increasingly being achieved with mass hilar stapling. Using the lateral approach with the spleen thus elevated, the surgeon can easily visualize the tail of the pancreas and avoid injury when placing the endovascular stapler. Once excised, the spleen is placed in a durable ripstop nylon sack, the neck of which is drawn through one of the 10-mm trocar sites. Morcellation of the spleen takes place within the sack and allows piecemeal extraction; a blunt instrument should be used to disrupt and remove the spleen to avoid the risk of sack rupture, spillage of contents, and subsequent splenosis [2, 23].

Figure 1 – Right lateral decubitus position and trocar positioning

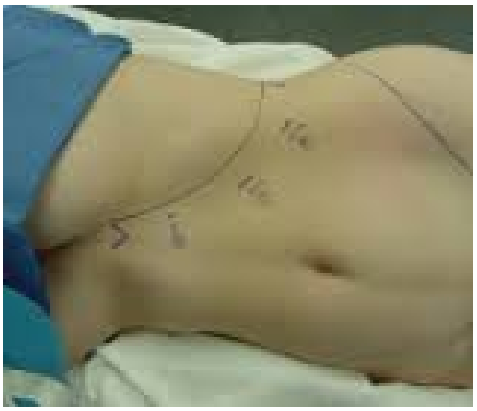

Figure 2 – Right lateral decubitus position and trocar positioning

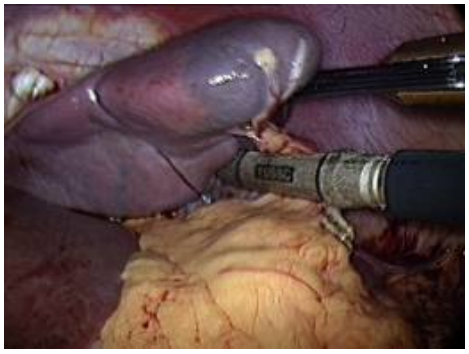

Figure 3 – Vital anatomy exposure of the spleen

Overwhelming Post-Splenectomy Sepsis

OPSS is rear but usually fatal complication, it has mortality rate of 50–60% even when treated [32, 33]. Occurs more often in immunocompromised adults and in children. 80% of cases are in first two years following splenectomy. It is caused mainly by encapsulated bacteria: Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae, other bacteria like Escherichia coli, Streptococcus b-hemolytic, Staphylococcus aureus and Pseudomonas sp. represent a significant risk as well [34]. Appropriate precautions and preventive measures are of importance, four measures consist the guidelines for prevention and treatment of OPSS: 1. vaccination with polyvalent pneumococcal vaccine 10–14 days prior elective splenectomy; 2. high risk patients (children and immunocompromised) should also receive vaccine against Haemophilus and Neisseria; 3. antibiotic prophylaxis (especially high risk patients); 4. early antibiotic treatment in signs of infection [2, 25, 35], Table 4.

Table 4

Guidelines for prevention and treatment of OPSS

	Guidelines for prevention and treatment of OPSS
1	Vaccination with polyvalent pneumococcal vaccine 10–14 days prior elective splenectomy
2	High risk patients (children and immunocompromised) should also receive vaccine against Haemophilus and Neisseria
3	Antibiotic prophylaxis (especially high risk patients)
4	Early antibiotic treatment in signs of infection

University Clinic for Digestive surgery -Skopje experience

Laparoscopic splenectomy (LS) was introduced I 2005 in our clinic. During 5 year period 2005–2010, 40 LS were performed for haematological disorders, other indications (trauma, malignant disease, other) included only 3 LS. Open splenectomy (OS) was analyzed in the period 2000–2010 and 21 OS were performed for haematological disorders in the period 2005–2010 and only 16 in the period 2000–2005, all together 37 OS in 10 years period. Main duration of surgery for LS was 166min and main hospitalization 6.8 days and blood transfusion 26 ml, Table 5 and 6.

Table 5

Patients undergoing splenectomy in the period 2000–2010

Diagnosis	Laparoscopic/Open surgery	Death
Haematological disease	40/37	0
Trauma	1/43	3
Malignant disease	1/21	0
Other	1/55	1

Table 6

Comparison between laparoscopic and open surgery in patients with haematological disease (2000–2010)

	Laparoscopic splenectomy n = 40	Open splenectomy n = 37
Duration of surgery (min)	166.1 ± 54.9	144.7 ± 48.8
Days of hospitalisation	6.87 ± 2.2	9.84 ± 2.9
Blood transfusion (ml)	26.2 ± 93.4	132.4 ± 252.3

Conclusion

Splenectomy for haematological disorders is only therapeutic and not curative, the relief of symptoms and for some disorders facilitation of chemotherapy leads to better quality of life and longer survival. Laparoscopic splenectomy is a procedure of choice when performed for haematological disorders and together with new imagine techniques decreased the need for diagnostic and staging splenectomies.

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Резиме

СПЛЕНЕКТОМИЈА ЗА ХЕМАТОЛОШКИ ЗАБОЛУВАЊА

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Спленектомијата претставува терапевтска метода за многу различни состојби. Причина за

тоа е либерализација на индикацијата и проширување на листата на болести подложни на спленектомија. Нарушувањата на црвената крвна лоза: автоимуна хемолитичка анемија, хередитарна свероцитоза, хемоглобинопатии и таласемија се болести кај кои се применува спленектомија по неуспешна медикаментозна терапија. Значително подобрување на тромбоцитопенија има кај најголем број тромбоцитопении по спленектомија, а најчеста индикација за спленектомија претставува ИТП (идиопатска тромбоцитопениска пурпура). Спленектомијата успешно го третира хиперспленизмот кај миелопролиферативните болести, се постигнува и намалување на симптомите од самата спленомегалија, но без ефект на неповратниот тек на болеста. Во болестите на белата крвна лоза (леукемија и лимфоми) спленектомијата има само палијативна улога, овозможува да се воведе хемотерапија.

Кај пациентите со хематолошки заболувања спленектомијата носи зголемен ризик од појавување на фулминантната и животозагрозувачка постспленектомиска сепса.

Иако спленектомијата кај хематолошките болести има само терапевтска, но не и куративна улога, намалувањето на симптомите кај некои нарушувања и воведувањето хемотерапија кај други доведува до подобар квалитет на животот и подолго преживување.

Клучни зборови: спленектомија, лапароскопска спленектомија, хематолошки заболувања, хередитарна сфероцитоза, идиопатска тромбоцитопениска пурпура, ИТП, миелопролиферативни болести, лимфом, постспленектомиска сепса.