LAPAROSCOPIC SPLENECTOMY IN THE TREATMENT OF HEMATOLOGICAL DISEASES OF THE SPLEEN

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LAPAROSKOPSKA SPLENEKTOMIJA

U LEČENJU HEMATOLOŠKIH BOLESTI SLEZINE

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ABSTRACT

SAŽETAK

Methods of surgical treatment of hematological diseases of the spleen have changed significantly in the past decade. The introduction of laparoscopic and minimally invasive procedures as standard for solving a significant number of conditions in abdominal surgery, has led surgeons to increasingly use laparoscopic surgery of the spleen. However, some unique anatomical characteristics of the spleen can lead to limitation in the application of laparoscopy. In this study, we investigated the application of laparoscopic splenectomy in the treatment of haematological disorders of the spleen, intraoperative and postoperative characteristics, the presentation of operational technique and the evaluation of the success of this procedure. In the treatment of benign hematological diseases, the effectiveness and efficiency of laparoscopy has been proven. The speculation of medical professionals is that laparoscopic splenectomy is an equal, if not the superior way of treating benign hematological diseases of the spleen in relation to the open procedure, and that there is a chance that laparoscopy might completely replace the classical surgery in most of it's indications.

Keywords: *laparoscopy, spleen, laparoscopic splenectomy, hematological diseases, ITP*

Modaliteti hirurškog lečenja hematoloških oboljenja slezine značajno su se promenili tokom poslednjih desetak godina. Uvođenje laparoskopskih i minimalno invazivnih procedura kao standardnih za rešavanje značajnog broja stanja u abdominalnoj hirurgiji dovela je do toga da hirurzi sve više primenjuju laparoskopske operacije slezine. Međutim, neke jedinstvene anatomske karakteristike slezine mogu dovesti do ograničenja u primeni laparoskopije. U ovoj studiji smo analizirali primenu laparoskopske splenektomije u lečenju hematoloških oboljenja slezine, intraoperativne i postoperativne karakteristike, prikaz operativne tehnike i procenu uspešnosti ove procedure. U lečenju benignih hematoloških oboljenja uspešnost i efikasnost laparoskopije je dokazana te je stav današnje stručne javnosti da je laparoskopska splenektomija ravnopravan, ako ne i superioran način lečenja benignih hematoloških oboljenja slezine u odnosu na otvorenu proceduru, te da postoji šansa da u budućnosti laparoskopija u potpunosti zameni klasičnu hirurgiju u većini njenih indikacija.

Ključne reči: laparoskopija, slezina, laparoskopska splenektomija, hematološka oboljenja, ITP

INTRODUCTION

The first splenectomy was performed by A. Zaccarelli in 1549. in Naples on a young woman due to splenomegaly (1). Quittenbaum did the first planned splenectomy in 1826. on a woman with liver cirrhosis and ascites (2). Hermann Schloffer, on the proposal of his then medical student, Kaznelson, in 1916. successfully performed splenectomy for idiopathic thrombocytopenicpurpura (3). The first laparoscopic splenectomy in adults was performed by Delaitre and Maignen in 1991 (4), and in children, it was done by Tulman in 1993 (5). In 2007. it was Prof. Slavko Matić at the First Surgical Clinic CCS, who first performed laparoscopic splenectomy in Serbia (6).



Corresponding author: Prof. dr Slavko Matić - hirurg Klinika za digestivnu hirurgiju - Prva hirurška klinika - KCS. The most common indications for laparoscopic splenectomy are idiopathic thrombocytopenic purpura (immunological thrombocytopenic purpura - ITP), (60-80% of all operated patients), followed by hereditary spherocytosis, autoimmune hemolytic anemia (AIHA), benign tumors and cysts, thrombotic thrombocytopenic purpura (TTP), Hodgkin's disease with malignant diseases at the end (7).

Idiopathic thrombocytopenia purport is an autoimmune hematological disorder, characterized by different degrees of thrombocytopenia (7). Surgical removal of the spleen (splenectomy) was the primary form of treatment for ITP until just over 50 years ago when the era of immunomodulatory therapy started (8). The significance of splenectomy is reflected in the fact that the spleen is not just the site of the most intensive degradation of damaged platelets, but also the site of antibody formation that opens the plateletmembrane, and prepares them for degradation (9). Since 1996. laparoscopic splenectomy has again become one of the main modalities of ITP treatment, while surgical treatment is considered in case of failed initialmedication therapy. Today, main indications for splenectomy in ITP are symptomatic splenectomy refractory to medical treatment, the need for high doses of corticosteroids to maintain remission, and relapses after initial response to steroids and the existence of contraindications to their use (10, 11).

So far, numerous advantages of laparoscopy have been demonstrated in relation to open surgery. Bettervisualization of the operating field is of particular importance since the spleen is a richly vascular organ, with numerous vascular relationships with surrounding structures (11). Clinical studies show a lower rate of mortality in laparoscopic splenectomy compared to open (12). Byimproving the technique and increasing the experience of the surgical team, the duration of the surgery is shortened (12, 13). Laparoscopy reduces thelikelihood of serious complications and therefore the need for reintervention (12, 13). Benefits of laparoscopy are also decreased intraoperative blood loss, fasterestablishing ofperistalsis, and lower need for postoperative analgesics, shorter recovery, and better cosmetic outcome (12, 13). The duration of postoperative hospitalization is also shorter, which reduces the overall cost of the treatment (11-13).

The goal of our study is to present a series of patients in whom we performed laparoscopic splenectomy for hematological diseases with the analysis of patient characteristics and outcomes.

MATERIALS AND METHODS

The first surgical clinic began to practice laparoscopic splenectomy began in 2007. Our study was conducted with 82 consecutive patients undergoing surgery at the IX Department of the Clinic for Digestive Surgery of the KCS -First Surgical Clinic in the period from 2007. to 2015. with alaparoscopic splenectomy for benign hematological diseases of the spleen only. All thepatients with malignancy were excluded, as well as those who had any kind of contraindications for laparoscopic surgery, such as prior abdominal surgery, extreme obesity or associated cardiovascular comorbidities. The study was performed as a retrospective case-series analysis of data obtained from thehistory of the disease. In all patients, the haematological diagnosis and primary treatment were provided by the hematologist.

All patients included in this study were primarily treated with medication therapy. Operative treatment decision, based on the above-mentioned demands, was obtained consilliary by the surgeon and hematologists. On the immediate preoperative preparation at the hematologist, there were 37 (45%) patients with an aim to increase the platelet count to> $50x10^{9}$ /L, and they were given pronison (prednisolon), IVIg, danazol, imuran (azithioprine) or some of the combinations of the drugs mentioned. Also, very important role in preoperative preparation, has vaccination in order to reduce the risk of infection by encapsulated bacteria (Streptococcus pneumoniae, Neisseria meningitidis and Haemophylus influenza).

Laparoscopic splenectomy is performed under conditions of general endotracheal anesthesia (OETA). After the patient is introduced into general anesthesia, a nasogastric tube is placed in order to decompress the stomach (11). The choice of approach depends on the operator, the size of the spleen, the anatomical characteristics of the patient and the eventual need for performing another procedure in the same act, for example, Cholecystectomy (13). More commonly, the right side (lateral) approach is practiced. This is theso-called hanging spleen technique (a technique of a hanging spleen), which implies that the patient lies on the right side of the operating table, while the body of the patient with the surface of the operating fieldcovers the of 45 to 75 degrees. The operating table is also adjusted so that the patient's legs are lower than the head, in the socalled, reversed Trendelenburgposition (11,12).

At the beginning of the operation, CO₂ insufflation is performed, creating pneumoperitoneum, which is maintained at 13-15 mmHG. Pneumoperitoneum exceeding 15mmHg can hemodynamically compromise the patient. Pressure inside is maintained <t constant levelsautomatically through the trocar throughout the procedure (7). There are four ports through which various laparoscopicinstruments are placed during the operation. The 12-mm diameter port extends left laterally from the anterior axillary line above the anterior superior iliac spine, since the stapler for dissection of the hylum is placed through it, and also discharges the splenic material at the end of the surgery. The camera is placed through a second port placed on the left and laterally from the umbilicus. The third is subxyphoid, and the fourth in the middle or posterior axially line under the left costal margin (11).

Placing the first trocar requires special attention, as it is the only part of the procedure that is performed blindly, before inserting the camera. When examining the abdomen (liver, lymph nodes, detection of eventual presence of accessory spleens), we begin by dividing the ligaments that hold the spleen in its position and in relationships with surrounding structures. The dissection proceeds with the division of the splenocolic ligament, which is cut by a laparoscopic ultrasound (Ultracission[®]), which provides us with access to the inferior pole of the spleen. We continue by cutting short gastric blood vessels, to approach the hylum of the spleen. Hilar arterial and venous blood vessels are most often handled with endovascular stapler, Hemolock' clips, titanium clips, and intracorporal ligatures, after which it is possible to relieve the spleen from other remaining ligaments (splenorenal, splenophrenic and splenogastric ligament) and thus completely separate it from its attachments. The left lateral trocar is then removed and through the same site we introduce polyethylene bag into which spleen is later placed. Inside the bag the spleen is fragmented withintention for easier extraction through trocar of the largest dimension. After rinsing the operative field and aspiration, it is necessary to re-examine the abdomen and insert surgical drain (3). Some authors believe that the drain is needed only in case of pancreatic injury, while others put it inroutinely at the end of each surgery (14). Nasogastric tube, placed before the surgical intervention, is removed after the establishment of intestinal peristalsis.

For classification of postoperative complications, the Clavien-Dindo Classification was used (15). Patients platelets were analyzed daily before surgery, as well as after surgery from the first postoperative day until the day of discharge. They were treated with low molecular weight heparin, with the addition of antiaggregation therapy in the case of an increase in the platelet count to over 500x10⁹/L. Corticosteroid therapy was gradually tapered until discontinuation.

The data was processed in the SPSS 20.0 program. The results are presented in the form of an arithmetic mean and standard deviation if they meet the criteria of normal distribution, otherwise they are represented by the median and the range of values. Categorical data are presented with absolute and percentage values. An X²test was used to analyze categorical type data. P values \leq 0.05 are determined as significant.

RESULTS

In the group of 82 patients operated by the laparoscopic method there were 15 (18.3%) men and 67 (81.7%) women. The mean age of the of our patients was (38.8 \pm 11.79) years (16-74). The average duration of hematologic treatment was 33.3 months (3 - 179). Most of the operatedpatients had a diagnosis of ITP-a 72 (87.8%), eight patients (9.8%) were diagnosed withspherocytosis, and two (2.4%) had diagnosis of AIHA. The average BMI was 24.3 kg/m² (18-30). The average platelet count was 81.8 (25-240) x 10⁹/L. Table 1: Types of used haemostatic techniques

Endo GIA	48	58.5%	< 0.001
Hemolock clips	27	32.9%	
Intracorporal ligatures	4	4.9%	
Titaniumclips	3	3.7%	

19 accessory spleens were detected intraoperatively, indicating their presence in 23.2% of the operated patients. For mobolization of the blood vessels of the hills of the spleen a. i v. lienalis (haemostatic technique), Endo GIA stapler with vascular filling, Hemolock^{*} clips, intracorporal ligatures and titanium clips were used. (Table 1)

Intraoperatively, the average blood loss was of 36.8ml (10-200) and average mass of the spleen fragmentsof 211.48 ± 32.73g (151-270). Of the total number of patients undergoing surgery, in 4 patients (4.9%) a conversion into an open procedure was performed, due to bleeding, in one patient due to an instrumental fracture of the spleen, in two due to a poorly placed Endo GIAstapler and one due to aninjury to the arteries for the inferior pole of the spleen. The average duration of the surgery was 83.6 minutes (48-135). In our group of patients, we postoperatively observed complications of (Grade I) in four of ourpatients, (Grade II) in six, one patient had complications of (Grade III), one of (Grade IV) and only one was found to have complications of (Grade V).In our group of operated patients, none of them had undergone reintervention. Median length of postoperative hospitalization was of 5.7 days (3-14). In one patient (1.2%), fatal outcome was recorded due to fulminant sepsis, after a series of non-surgical complications. The therapeutic response was complete in 60 (74.1%) patients. In 18 of them, additionaltherapy was required, and in 3 patients, the therapeutic response proved to be poor. (Table 2)

Table 2: Perioperative characteristics and patient outcomes

Characteristics	average	min	max	
Intraoperative blood loss in ml	36.8	10	200	
Duration of surgery in min	83.6	48	135	
Length of postoperative hospital stay in days	5.7	3	14	
Complications, n (%)				
Ι	4 (30.8)			
II	6 (46.1)			
III	1 (7.7)			
IV	1 (7.7)			
V	1 (7.7)			
Therapeutic response, n (%)				
Complete response	60 (74.1)			
Additional therapy	18 (22.2)			
Poor therapeutic response	3 (3.7)			
Death	1(1.2)			

DISCUSSION

The objectives of laparoscopic splenectomydefined in 1991. when the first intervention was made, were: Maintain results identical to open surgery in terms of efficacy and safety, while reducing the trauma of the abdominal wall, easier postoperative recovery, shorter duration of hospitalization (16).

Laparoscopic splenectomy was quickly accepted by medical professionals and became widely applicable worldwide. This enabled analyzing the results obtained from different studies, that follow an increasing number of these interventions, easier. With the purpose of answering the question of whether the application of laparoscopic splenectomy is really justified?

Delaitre et al. analyzed 209 patients who were treated almost exclusively by laparoscopy in a study conducted at the level of 12 surgical centers in France (12). The Japanese study of Wu and associates analyzed 10 patients over a five-year period and the aim of the study was to examine the effectiveness of laparoscopic splenectomy, as well as the safety and benefits of using this technique in the treatment of ITP in patients with an extremely low platelet count (<1x10⁹/L), which explains the small number of subjects involved in the study (17).

The results of our study show that hematological disorders of the spleen were more common in female subjects with incidence of 81.7% compared to men with 18.3%. The average age of patients in our group was 38.8 years (16-74). Based on the analysis of demographic characteristics, which include the age and gender of patients, we can say that the results we obtained do not differ significantly from the data found in literature.

Patients included in our study were cared for by their hematologist before being subjected to surgical intervention. The period of medication treatment ranged on average 23.5 months (3-420). Wu et al. calculated that in their patients, the average age of patients at the time of diagnosis was 21.5 (9-43) years, while at the time of surgical intervention they were 32.6 (15-62) years (7). The authors do not state that the time from diagnosis to surgery could be significant for the possibly different outcome of treatment, but we may conclude on the basis of the results that show that all patients, even at the last checkup performed after 36 months, had a value of platelets > $100x10^9$ /L (in one patient the value was $126x10^9$ /L, in one $154x10^9$ /L, and for the remaining eight patients, the value was over $200x10^9$ /L) (7).

In the study of Elezović and colleagues, the patients age at the time diagnosis ranged from an average of 35 years (17-74), and splenectomy was commonly performed within 12 months (2-160). The results showed that the occurrence of remission did not depend on the time elapsed from diagnosis to surgical intervention (8). The majority of our patients of interest received corticosteroids, mainly prednisone, and less commonly urbason and methylprednisolone, while other drug options such as, combinations of predni-

sone and IVIg, danazol or immuran, were reserved for refractory forms of the disease. According to The American and British society of Hematology ITP Treatment Guide, Corticosteroids and ivIg should be an initial treatment option, or should have priority over splenectomy (13). A study by Dolan and associates analyzed some of the attempts to avoidsplenectomy as a treatment option in patients who did not have an adequate response to steroids, by using new therapeutic options like anti-D antibodies and anti-CD20 antibodies. Ultimately such treatment turned out to be inferior to splenectomy (5). In our group of patients, the platelet number on the admission was 81.8×10^9 /L (25-240) on average. Thrombocyte values of over 100 x 10⁹/L have been seen in some cases and are the consequence of the use of medication therapy prescribed by the hematologist with an intention to prepare patients for the surgical intervention. In the French study, Delaitre and Associates, the mean platelet count was 92.7 x 10⁹/L, ranging between 3 and $444 \ge 10^9$ /L. In this study, as many as 178 out of 209 patients underwent preoperative preparation, which explains this high value of platelets before surgery (3).

The first intraoperative characteristic analyzed in our study was the detection of accessory spleens, which were observed in 19 patients. They were most commonly found (in cases where there were more than one) in the hylum, gastrocolic ligament, omentum, the tail of the pancreas. The first major study on the effectiveness of the detection of accessory spleens in patients operated with classic open technique and a laparoscopic approach was published by Samphat and Associates (2007) (9). Today's impression of laparoscopy is that it does not lag open surgery regarding the possibility of intraoperative detection of accessory spleens.

According to our study, mean intraoperative blood loss during laparoscopic splenectomy was 36.8 ml (10-200), whereas in the study of Park and associates, the mean blood loss was 162 ml (5-1400) (17). Amongst many data found in literature, maybe the best indicator of the safety and benefits of laparoscopyare the study by Wu and associates, which states that the blood loss in patients operated by the laparoscopic technique ranged on average 44 ml (10-100) (7). Adding to thisthe fact that this was a group of vulnerable patients, in which even the lowest blood loss could be fatal, we can see the real significance in their treatment.

In the majority of patients, hilar vessels are divided with Endo GIA stapler with vascular filling at 48. In 27 patients, Hemolock clips were used, in four, intracorporeal ligatures and in three patients, we used titanium clips. Habermaltz and associates cite bleeding as the most significant intraoperative complication and the most common reason for conversion to an open procedure. They also recommend the use of endovascular staplers for the treatment of blood vessels of the hylum of the spleen, instead of ligatures or clips, on the basis of studies that have shown that this can prevent bleeding during and after intervention (14). Dolan and associates listed the use of an endovascular stapler as a standard in the treatment of hilar spleen vessels (5). Park and associates expressed an opinion, that the application of endovascular stapler should be given priority over the clips. This paper states that the bag for the extraction of the spleen, is an integral part of the equipment for the laparoscopic splenectomy, and is to be used whenever possible (17). In our study, we used these bags in all the patients, except for when conversion to an open procedure was done.

In our study, the conversion to open procedure was performed in 4 patients (4.9%) due to bleeding, which was also the only type of complication recorded. In one patient, due to instrumental rupture of the spleen, a conversion was made, in one due to an injury to the arteries for the inferior pole of the spleen, and in two of them due to a poorly placed Endo GIA stapler (the stapler was caught in the clips previously placed on surrounding smaller blood vessels). In France, the study of Delatrie and associates, conversions were performed in 17.2% of the operated patient, and the cause was, in all cases, bleeding (3). There were no conversions in the Japanese study of Wu and associates in 10 operated patients (7). Park and associates published a study in 2001. which also included results of laparoscopic splenectomies in the period 1995-1999, performed by 14 surgical teams, each of which had a sample of at least 24 patients. Only one sample of 49 patients did not make a conversion. All other authors recorded a certain percentage of conversions ranging from 3 to 19% (17). What is to be expected, is that the percentage of conversions into an open procedure is reduced by gaining greater experience and skills, but one should not forget that the type of pathology in question and the size of the spleen are of great importance when considering this problem. In the US National Registry, from 2005 to 2010, 37006 splenectomies were recorded, showing a worrying 22.5-33.9% of conversion, with only 13.3% of patients being treated with laparoscopic technique (18).

According to our results, the average duration of surgery was (83.60 ± 14.75) minutes (48 - 135). In the previous years, the length of laparoscopic splenectomy was much longer. That can be seen from manypublished studies, amongst which is the one published by Delaitre and associates, where the average duration of surgery was 144 minutes. The authors of this study concluded that the experience of the surgical team was one of the most important factors. It greatly influenced the duration of laparoscopic intervention and predicted its shorter duration with the acquisition of the necessary experience (3).

In the study of Delaitre and associates, 209 patients were treated laparoscopically, and three patients required reinterventions. In two of them, because of bleeding and in one the cause was pancreatitis (3). Unlike theirs, our study and the study of Sampath and associates did not have a single reintervention (9), but we should bear in mind that Delaitre had many more patients, so it is expected that the number will be higher.

For the evaluation of postoperative complications, in our group of operated patients, Clavien-Dindo classification was used (15). In one patient, fatal outcome was recorded due to fulminant sepsis after a series of nonsurgical complications (Grade I). In one patient, myocardial infarction (Grade IV) was recorded. Percutaneous drainage for necessary collection after surgically removed spleen (Grade III) was performed in one. In six patients, additional antibiotic therapy was required (Grade II), and four patients needed additionaltherapy in the form of antiemetics, analgesics and antipyretics (Grade I). Literature indicates a significantly lower percentage of postoperative complications in patients undergoing laparoscopic surgery compared to an open one. Winslow and Brunt together with collaborators worked on a meta-analysis of 51 series with a total of 2940 patients (2119 of them were laparoscopic splenectomies and 821 open procedures) and showed a statistically lower percentage of complications in the laparoscopic group, which was 15.5% compared to 26.6% in the open procedure group (19). Postoperative complications in the study of Delaitre and associates occurred with a frequency of 8.7%, while in the case of an open procedure, due to bleeding during the operation, it increased to as much as 19.4% (3).

The average duration of postoperative hospitalization was, in our patients, 5.7 days (3-14), in the study by Delaitre and associates, it was found to be 5.1 days (12), and in the study by Wu and associates, 6.8 days (4-9) (7).

In our study, the drain was placed at the end of all surgical procedures. Delaitre and associates placed the drain in 72.3% of the patients and they also recorded a higher morbidity of 13.7% in that group, compared to the group of 5% of patients where drain was not inserted. But no statistical significance was proven (3). Habermalz and associates state that there is still no clear position regarding the use of drainage after laparoscopy and that it is the decision on the operator, except in cases of suspicion of pancreatic injury when drainage is certainly required to be placed (14).

According to our results, a good therapeutic response was found in 60 patients (74.1%), moderate response, ie the need for additional therapy, in 18 patients (22.2%) and 3 patients had poor therapeutic response (3.7%). In 2008. The European Association for Endoscopic Surgery clinical practice guideline published that the authors of certain studies (Trias et al. Cordera et al. Lozano-Salazar et al.) managed to prove that long-term results were identical in laparoscopic and classical surgical patients (11). Dolan and associates classified the results of 5 studies, which compared patients with laparoscopic surgery and a classic approach and concluded that there was no statistically significant difference in either of these studies (5). The experts think that laparoscopy is at least as effective, if not more effective, in the treatment of ITP and other benign hematological diseases of the spleen, as well as open surgery.

As our study is presented as a case-series of 82 patients, we still should be cautious about drawing conclusions, and further prospective randomized analyses should be performed. Possible other limitations that should be noted are in regard of multiple hematological diseases for which the patients were operated, andrelatively short follow-up period.

Today, 26 years after the first laparoscopic splenectomy in adult patient was presented to the medical public, the chances of laparoscopy, completely replacing conventional surgery in the future in most of its indications, are high. Even so, this does not exclude the need for new research papers to compare the outcomes of the laparoscopic and classic procedures, however there is a problem related to laparoscopic treatment of malignant diseases of the spleen in the presence of splenomegaly and problems with manipulation of the spleen in the operative field. Even if laparoscopic splenectomy will not become broadly accepted in the surgery of malignant diseases of the spleen, there remains a wide spectrum of benign hematological diseases where the effectiveness and efficiency of laparoscopy is proven. It can help this large group of patients not only by treating their illness, but also, by reducing the trauma of the body, which will result in faster recovery, and all along with a better quality of life.

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