ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:
‘‘ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,
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ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
ΙΑΤΡΙΚΗ ΣΧΟΛΗ

ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

ΘΕΜΑ:

THE USE OF SINGLE INCISION LAPAROSCOPIC SURGERY IN SPLENECTOMY

ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:
ΚΟΥΡΟΥΜΠΑΣ ΕΥΣΤΡΑΤΙΟΣ
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ΠΡΑΚΤΙΚΟ ΚΡΙΣΕΩΣ
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Του Μεταπτυχιακού Φοιτητή Ευστράτιου Κουρουμπά

Εξεταστική Επιτροπή

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- Θεόδωρος Διαμαντής, Καθηγητής Χειρουργικής

Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε από την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της .....ης ..... 20.... για την αξιολόγηση και εξέταση του υποψηφίου κου **Ευστράτιου Κουρουμπά**, συνεδρίασε σήμερα .../.../....

Η Επιτροπή διαπίστωσε ότι η Διπλωματική Εργασία του Κου **Ευστράτιου Κουρουμπά** με τίτλο: «The use of single incision laparoscopic surgery in splenectomy», είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ..... προτείνει την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's Degree), στον παραπάνω Μεταπτυχιακό Φοιτητή.

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ....., και για τον βαθμό «ΚΑΛΩΣ» ψήφους ..... Κατά συνέπεια, απονέμεται ο βαθμός «.....».

Τα Μέλη της Εξεταστικής Επιτροπής

- Ιωάννης Γκρινιάτσος, Επιβλέπων (Υπογραφή) _____
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Αφιέρωση

‘‘ Στην Σύζυγο μου για την υποστήριξη της και για το μεγαλύτερο δώρο που μου έκανε ποτέ κάποιος, τον γιο μας’’

Ευχαριστίες

Θα ήθελα να ευχαριστήσω ιδιαίτερα τους Διευθυντές και Επιμελητές του Β' Χειρουργικού τμήματος του Τζανείου Νοσοκομείου Πειραιά κυρίους:
Γεωργιάδη Φοίβο , Παρασκευά Μάριο, Κοντοστόλη Στυλιανό, Σφηκάκη Πέτρο ,
Γεώργιο Αγιομαμίτη και Βλαχάκο Νικόλαο , για την υπομονή τους και την επιμονή τους στην εκπαίδευση της Χειρουργικής αλλά και των ηθικών αξίων της Ιατρικής στην μακριά πορεία της ειδικότητας .
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Contents

PART ONE

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Introduction

Spleen is one of the most important viscera of the human body. It is a cardinal organ on the size of the palm. Some of the basic functions are to protect the body against viral infections; to filter the blood products and to keep the robustness of the circulation. On the other hand splenectomy is an operative procedure indicated – except from trauma – for a variety of hematological diseases, benign or malignant.

Depending on the nature of the disease, splenectomy can be applied for diagnostic or staging purposes and as a therapeutic measure in order to achieve cure or amelioration of symptoms. In the last decades, indications have been changed because of the improvement of diagnostic and therapeutic protocols. Spleen surgery has been altered nowadays upon the introduction of laparoscopic techniques.

Laparoscopic splenectomy is currently the gold standard for the treatment of patients when surgical resection is indicated. Despite the lack of evidence - based on double blind randomized studies - about the superiority of laparoscopic method, according to worldwide consideration laparascopic splenectomy has managed to achieve the standard advantages of the laparoscopic interventions (postoperative pain, rehabilitation, aesthetic outcome) while still safe and efficient as the open resection.

Single Incision Laparoscopic Surgery (SILS) is a modification of standard laparoscopic procedure, using the same instruments which have been applied on a variety of operations. There are few case reports of single incision laparoscopic splenectomy. The scope of this study is the bibliographic review of laparoscopic splenectomy concurrently with the analysis on patient's outcome.

1. Spleen

1.1. Anatomy and histology

The spleen is situated principally in the left hypochondriac region, but its superior extremity extends into the epigastric region. It lies between the fundus of the stomach and the diaphragm. (Figure 1.1)

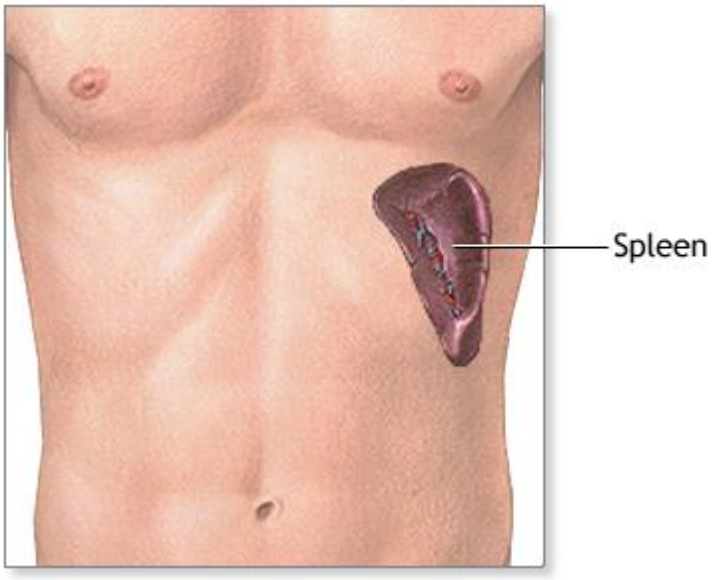

Figure 1.1 Topographic anatomy of the spleen

The size of the spleen is liable to very extreme variations from tetrahedron to coffee bean depending on the size of the colic imprint. Its horizontal axis lies on the 10^{th} rib line while its posterior margin is located 3, 5 to 4cm further from mid-dorsal line opposite to 10^{th} thoracic vertebra. Its anterior margin reaches the axillary line.

It's soft, of very friable consistence, highly vascular and of a dark purplish color. It comprises of diaphragmatic and gastric surface, superior and lower extremity, anterior and posterior border. The diaphragmatic surface is convex, smooth, and is directed upward, backward, and to the left, except at its upper end, where it is directed slightly medial ward. (1)

It is in relation with the lower surface of the diaphragm, which separates it from the ninth, tenth, and eleventh ribs of the left hemi thorax. The visceral surface is directed to the visceral cavity and divided by a ridge into an anterior or gastric and a posterior or renal portion. (Figure 1.2)

The gastric surface , which is directed forward, upward, and medially, is broad and concave and is in contact with the posterior wall of the stomach, from which is divided by a portion of great omentum. It presents near its medial border, a long fissure termed the hilum. This is pierced by several irregular apertures, for the entrance and exit of vessels and nerves.

The renal surface is somewhat flattened, located on the lower portion of the gastric surface from which is divided by a prominent margin. It is in relation with the upper part of the anterior surface of the left kidney and occasionally with the left suprarenal gland.

The superior extremity is directed toward the vertebral column, where it lies on a level with the eleventh thoracic vertebra.

The lower extremity or colic surface is flat and rests upon the left flexure of the colon and the phrenicocolic ligament and is generally in contact with the tail of the pancreas. The anterior border is convex and often notched, especially below; indicating its lobular consistence during the early embryonic development.It separates the diaphragmatic from the gastric surface.

The posterior border is more rounded than the anterior, separates the renal from the diaphragmatic surface; it corresponds to the lower border of the eleventh rib and lies between the diaphragm and left kidney.

The inferior border is usually rounded and blunt, heading to the spine.

The anterior border rests upon the left flexure of the colon and the phrenicocolic ligament. The spleen is almost entirely surrounded by peritoneum, which is firmly adherent to its capsule. There are folds of the peritoneum between the stomach, the spleen and the left kidney. Spleen is held in position (connected to the stomach and posterior abdominal wall) by two folds of this membrane. One, the phrenicolienal ligament, is derived from the peritoneum, where the wall of the general peritoneal cavity comes into contact with the omental bursa between the left kidney and the spleen; the lienal vessels pass between its two layers. The other fold, the gastrolienal ligament, is also formed of two layers, derived from the general cavity and the omental respectively, where they meet between the spleen and stomach.

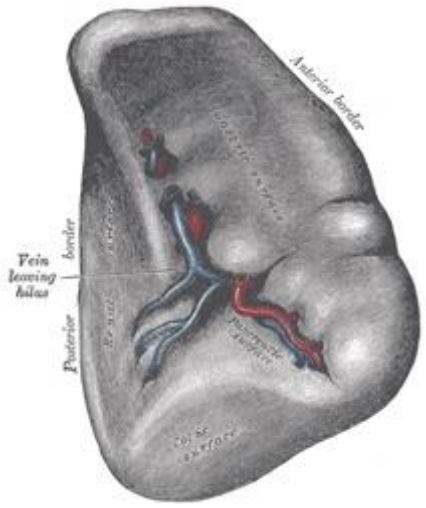

Figure 1.2 Visceral surface of the spleen

The short gastric and left gastroepiploic branches of the lienal artery run between its two layers. (Figure 1.3) The lower end of the spleen is supported by the phrenicocolic ligament.

The size and weight of the spleen are liable to very extreme variations at different periods of life, in different individuals, and in the same individual under different conditions.

In the adult it is usually about 12 cm. in length, 7 cm. in breadth, and 3 or 4 cm. in thickness but tends to reduce in size and weight during lifetime. Weighs about 150 grams, varying from 80 to 300 grams depending on its blood load. (2) The size of the spleen is increased during and after digestion, and varies according to nutritional status of the body. (3)

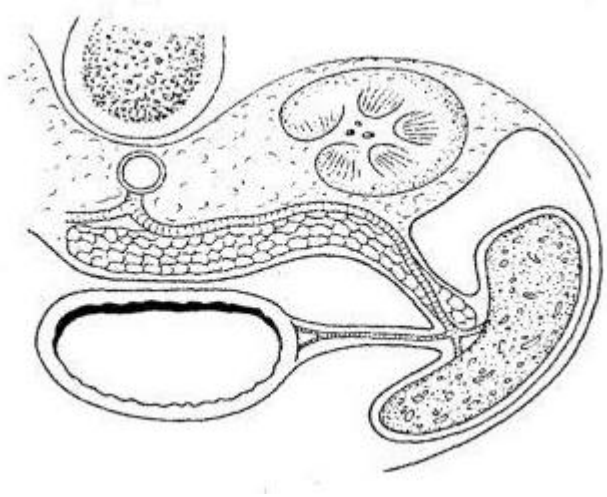

Figure 1.3 Anatomic relations of spleen vessels

Frequently in the neighborhood of the spleen, and especially in the gastrolienal ligament and greater omentum, small nodules of splenic tissue may be found, either isolated or connected to the spleen by thin bands of splenic tissue. They are known as accessory spleens (*lien accessorius; supernumerary spleen*). (Figure1.4)

Spleen could maintain its embryonic lobular consistence or accommodate deep fissures on diaphragmatic surface except from superior margin. The location of the spleen can be identified by percussion. The area of dullness extends between the 9^{th}, 10^{th} ,11^{th} rib and the medial axillary line. Normally spleen isn't palpable.

Despite the simple external anatomy of the spleen, its inner structure is rather complicated. Peritoneum invests the spleen and is adherent to fibro elastic coat..The fibro elastic coat (*tunica albuginea*) also invests the organ, and at the hilum is reflected inward upon the vessels (splenic artery and vein) in the form of sheaths.

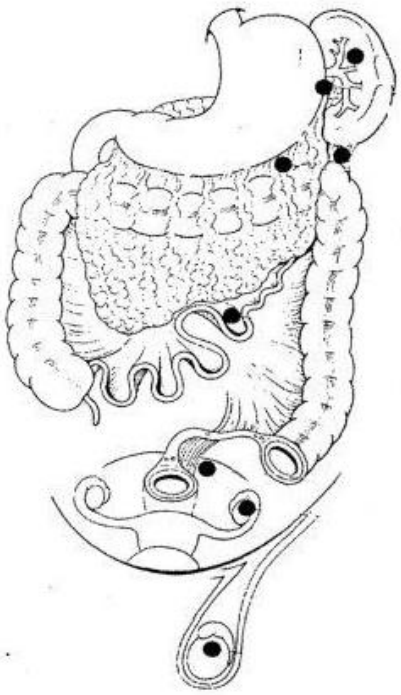

Figure 1.4 Possible locations of accessory spleens

From these sheaths, as well as from the inner surface of the fibro elastic coat, numerous small fibrous bands, trabeculæ are given off in all directions; these uniting, constitute the frame-work of the spleen. The spleen therefore consists of a number of small spaces or areolæ, formed by the trabeculæ; in these areolæ is contained the splenic pulp. (4)

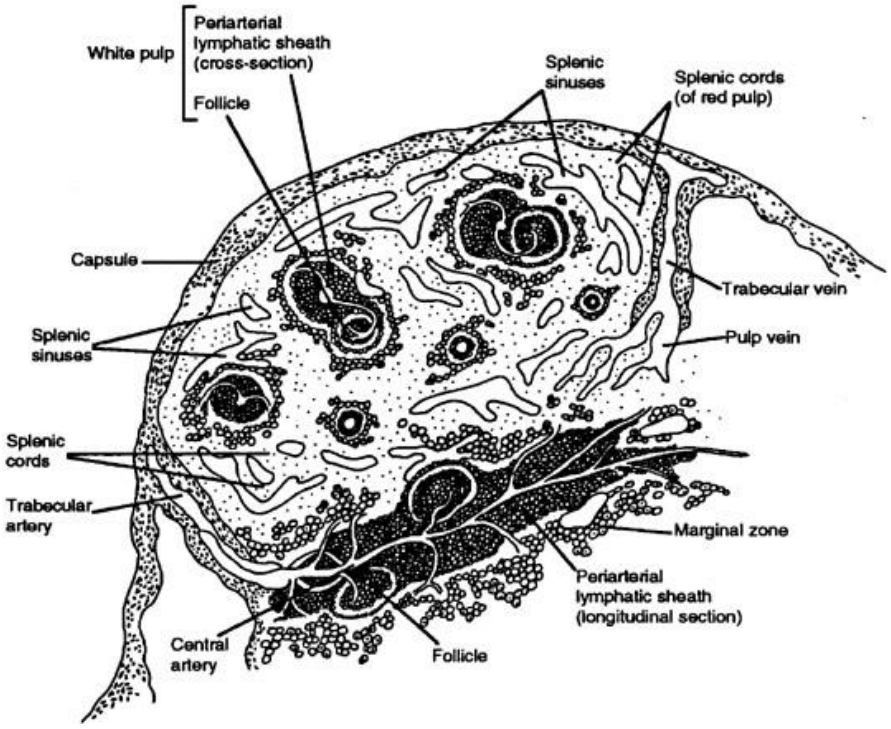

Figure 1.5 Cross section of the spleen

Splenic pulp is the functional portion of the spleen. In a vertical cross section the spleen consists of white and red pulp. Red pulp has some darkish regions. Spleen is surrounded by a capsule composed of dense fibrous tissue with elastic and smooth muscle fibers whose contraction facilitates the blood circulation. (5)

Starting from the external coat of the hilum, fibrous trabeculae are headed towards the interior of the organ serving as a guide of the vessels.

Splenic artery is divided in 4 – 5 branches at the hilum that are divided again before entering the organ. Each of these branches .

Following a short route, the artery is separated from the vein still remaining inside the trabeculae , while the vein exits the trabeculae and entrains the parenchyma. The artery continues its course, consecutively dividing in branches until reaching a diameter of 0,2mm (final arterioles) where exit the trabeculae and enter the red pulp.

Nerves follow the same route and terminate to the same point. Recently was discovered that the pulp lacks of nerve fibers. Arterioles upon exiting the trabeculae enter the Malpighian splenic bodies, which constitute the white pulp. These rounded bodies have

lumphnodular consistence and are made from reticular tissue and lumphatic cells. Their center includes large lymphatic cells (Thymus depended T lymphatic cells).

These lymphatic cells have nuclear differentiation. Splenic bodies are true lymphocytogenic formations that produce lymph cells which enter the bloodstream through the meshes of red pulp's reticulum.

These periarteriolar lymphatic formationsare located near the extrusions of the splenic coat forming the white pulp. They consist of 15% the spleen's size and 25% of body's lymphatic system. It's considered that the splenic corpuscles produce also specific antibodies and their size increase proportionally to antigenic stimuli.

The lienal artery is remarkable for its large size in proportion to the size of the organ, and also for its tortuous course. It divides into six or more branches, which enter the hilum of the spleen and ramify throughout its substance . These ultimately leave the trabecular sheaths, and terminate in the proper substance of the spleen in small tufts or pencils of minute arterioles, which open into the interstices of the reticulum formed by the branched sustentacular cells. Each of the larger branches of the artery supplies chiefly that region of the organ in which the branch ramifies, having no anastomosis with the majority of the other branches.The arterioles, supported by the minute trabeculæ, traverse the pulp in all directions in bundles (*pencilli*) of straight vessels. The capillary vessels of 5 microns diameter, without sheath entrain the reticular tissue (red pulp) and terminate directly to the venous sinuses or the red pulp. The pulp consists of trabeculae like hepatic lobe and connective reticular cells. That network contains white blood cells, red blood cells, platelets and large lymphoid cells.

White pulp merges with the red pulp on its circumference (marginal zone), which constitutes the 80 – 85% of the spleen. It is considered that the lumen of the venous sinus communicates with the reticulum of red pulp so that blood comes through this network to the venous sinuses. Longitudinal endothelial cells are lined on the wall of venous sinus, forming small apertures through which the aforementioned communication is possible. (6)

Coronary fibers originating from red pulp's connective tissue hold together these longitudinal cells. Like the lymphoid cells have phagocytic and pooling properties and along with hepatic Kupfer cells are considered the most important factors of reticuloendotheliac system. Tuft arterioles expand while entering the red pulp so that the

blood flow reduces permitting sequestration of harmful substances and destruction of senescent red blood cells by the reticular cells and macrophages that come in contact.

Billroth Th. first described the red pulp in 1854 and denoted the venous sinuses, thus the perivenous network is called Billroth network. The smaller veins unite to form larger ones; these do not accompany the arteries, but soon enter the trabecular sheaths of the capsule, and by their junction form six or more branches, which emerge from the hilum, and, uniting, constitute the lienal vein, the largest radicle of the portal vein.

Lymphatic vessels starting from the white pulp travel towards the hilum parallel to the other vessels and terminate on the local lymphnodes. There is also a superficial lymphatic network around the coat of the spleen.

1.2. Physiology of the spleen

Spleen is the unique lymphnodal tissue specified in filtering blood and has a lot of functions immunological or not. Removes infected or destructed cells from circulation , converts hemoglobin to bilirubin and recycles ferrum. (Table 1.1)

Like other lymphnodes is a part of peripheral lymphatic – specific system, produces lymphoid and plasma cells and participates in specific immunological procedures especially in the first years of life where other parts of lymphatic system haven't been developed. (7)

Splenectomy is followed by serious bacterial infections not only in the newborns but also in adolescents and adults. Spleen is covered by coat of connective tissue that is reflected inwards in the form of sheaths. Splenic parenchyma consists of red and white pulp. White pulp has lymphnodules that produce lymphocytes .Blastic centers and arterioles in the white pulp are considered as thymus - depended areas. Red pulp invests the white pulp and contains a large number of red blood cells because of blood filtering. Arterial blood enters through the hilum, reaches the small arteries surrounded by lymphocytes (white pulp) and terminates to capillaries that pass through the lymph nodules. Red pulp has components of the reticuloendothelial system that participate in phagocytosis. Beyond that, spleen can be immunological stimulated by antigenic presence. (7)

Table 1.1 Splenic Physiology

Splenic Physiology	
Reticuloendothelial system	Blood filtration
	Phagocytosis
Vascular	Blood pooling
	Hemodynamic contribution to portal circulation
Lymphatic	Immune response
	Cellular
	Humoral
Heamopoiesis	Fetal site of haemopoiesis
Metabolic	Lipid degradation
Secretive	Production of coagulation factors
	Reserve pool for platelets

1.2.1. Immune response

According to the current perception immune response implements three basic functions: Defense – Homeostasis – Vigilance. Defense manifests as the resistance against bacterial infections. Homeostasis refers to the ability of the body to remove damaged cellular components circulating in the bloodstream. Vigilance has to do with identification and destruction of mutant cells.

Whether the cellular components of defense correspond successfully, the body will dominate against the bacteria. But if the aforementioned components overact, undesirable manifestation may occur, like allergy or hypersensitivity. Deviation from homeostasis causes an autoimmune condition.

The third function of immune system is recently acknowledged and refers to the identification and destruction of abnormal cellular types. Failure of that function is related to development of malignant neoplasms.

Immune response, in the aspect of specificity can be classified on two categories: Non specific and specific immune response.

1. Non specific immune response: inflammation and phagocytosis.

First contact of the body with a extrinsic antigen leads to stereotype response that consists in activation of phagocytes on the entry points. This can be done solely or as part of a generalized inflammatory response.

2. Specific immune response

Specific immune response refers to identification and final investigation of the hostility of the antigen with a very specific procedure. The result of the contact between the body and the antigen depends on the properties of the substance (size, structure, chemical compound, quantity) and the body respectively (age, genetic origin)

Three characteristics can distinguish the non specific from specific immune response:

1. Specificity. It is a highly selective attribute according to which, the products of the immune response will interact solely with the antigen that caused the response.

2. Eterogenity. Refers to a number of cellular locations and products that counteract with each other in order to produce a variety of immune responses. This heterogenity of cellular types produces an also heterogenous population of cellular products e.g. antibodies.

3. Memory. Is the ability that contributes effectively in an accelerated and dynamic immune response through proliferation and differentiation of activated cells by the presence of an antigen.

Two types of mechanism can promote the specific immune response:

1. Humoral immunity based on cellular component of lymphatic tissues called antibodies

2. Cellular immunity based on specifically stimulated lymphocytes.

1. Humoral Immunity

Humoral immunity is promoted by a group of lymphocytes that differentiate in bone marrow and referred as bone marrow derived or B lymphocytes. The antibody is a product of B cells (B-lymphocyte or plasmatocyte) and is connected with the cells or secreted as extracellular product. It has the ability to react with the antigen responsible for its production. Antibodies in human reflect 5 major groups of proteins – the immunoglobulins that vary in size, biological attitude and biochemical functions.

2. Cellular Immunity

Cellular immunity is promoted by a group of lymphocytes that differentiate under the affection of thymus gland and referred as T lymphocytes. That segment of specific immunity is implemented by specifically stimulated lymphocytes or special cellular products that are produced by the reaction of the antigen with specific stimulated lymphocytes known as lymphokines. Lymphokines include the leukocyte migration inhibitory factor, cytotoxin, interferon and others that make up the compounds of cellular immunity.

1.2.2. Circulation and blood filtering

Spleen acts as a filter of the circulating blood by removing erythrocytes and damaged cells. Erythrocytes can be purged of disintegrating mitochondria, ferric granules and infectious agents. In order to maintain all these functions, spleen should have adequate blood flow. Actually, six per cent of the cardiac output passes through the spleen (aprox. 300ml/min). On a spleen of normal weight the amount of blood is 3ml/min/kg but this flow index reduces on enlarged spleen.

Blood passing through the spleen is directed towards the mesh of the red pulp rather than the channel artery – arteriole – tuft arteriole – capillary – sinusoid – vein. Seemingly, there are two circuits of circulation that are supported by two theories, the closed circuit that is shorter and the open that is more significant.

The way that spleen distinguish the different kind of cells , is rather simple. Large, abnormal cells (spherocytes) are hard to pass through the apertures of the red pulp towards the sinusoids, so are being entrapped and destructed.

Blood flow deceleration is the most important fact for the sequestration in the mesh of the red pulp. Senescent or abnormal cells are destroyed there because of the osmotic pressure gradient while the permeability of the membrane is also important. This procedure is an active purging not a passive apoptosis.(8) Experiments have proved that senescent erythrocytes are discarded exclusively at the spleen.

Spleen has also vital role in iron metabolism. Until 5th fetal month spleen is an important haemopoietic organ but afterwards ceases and bone marrow takes over. If the bone marrow loses his haemopoietic ability, spleen could act as a center of extramedullaryhaemopoiesis

In animals such as the dog, cat, horse and guinea-pig a considerable amount of blood is stored in the spleen. Conversely, in healthy adults spleen doesn't work as a blood pool, but accommodates 1/33 of platelets that can be restored to the circulation when needed. That attribute can be a problem when an enlarged spleen causes thrombocytopenia. Platelets degradation undergoes in the spleen.

The hemodynamic contribute of the spleen in the portal vein system is not entirely comprehensible. Some researchers consider spleen as the "heart" of portal circulation. Based on canine experiments, portal vein flow can be augmented as much as 200% in case of hypoxia and this is due to the opening of arteriovenous channels in the spleen.

The same mechanism can explain the painful feeling on the left upper abdominal quadrant after tortuous exercise. It is considered as ischemic stroke. Another issue is the relation between thrombus formation and the spleen. Most of the products needed for a thrombus to be formed are mobilized by the spleen. Factor VIII is either produced or stored in the spleen.

2. Splenectomy

2.1. Indications

Splenectomy is a procedure indicated either for traumatic spleen injuries or a variety of hematological diseases malignant or bening.

Splenectomy ,depending on the nature of the disease can be done either for diagnostic and staging purposes or as treatment in order to achieve cure or symptoms relief.

The indications of splenectomy have been changed in the last decades because of the evolution of diagnostic techniques and treatment protocols. The extent of spleenectomy (total or partial) depends on the underlying hematological condition and the indication for resection.

The effectiveness of splenectomy has been established for Idiopathic Thrombocytopenic Purpura. The decision of splenectomy for lymphoproliferative disorders or myelohyperplastic malignancies is still debatable and the possible outcome is questioned. This is because complications and mortality are higher in malignancies, but has to do with higher age, poor health condition or previous immunosuppressive remedies.

Splenectomy is required for the following reasons:

1. intense enlargement
2. overactivity
3. autoimmune disease
4. diagnostic and therapeutic purposes

Major indications for splenectomy include:

a. Hereditary Spherocytosis
b. Idiopathic Thrombocytopenic Purpura
c. Autoimmune Hemolytic Anemia
d. Splenomegaly if there are underlying clinical symptoms

Rare indication is the Hodgkin disease and some forms of non Hodgking lymphomas. Splenectomy on patients with other conditions is controversial but can be done under circumstances. These include homozygous b – thalassemia and other hemoglobinopathies, hemolytic anemias, chronic myelogenous leukemia, myelofibrosis and polycythemia vera.

Table 2.1 Major Indications of splenectomy based on treatment protocols Haematologica 1999; 84: 431-436)

Years								
	HS	**AHA**	**ITP**	**MF**	**NHL**	**CLL**	**HCL**	**HD**
	%	%	%	%	%	%	%	%
Always	95	0	0	0	0	0	0	0
Often	5	100	100	72	98	72	49	32
Rarely or never	0	0	0	28	2	28	51	68
Resistance to therapy	-	95	79	2	0	8	30	0
Dependence to therapy	-	0	17	0	0	0	0	0
Bleeding	0	0	17	0	0	0	0	0
Intense thrombocytopenia	0	2	30	8	15	15	4	0
Intense anemia	5	0	0	21	15	19	2	0
Spleen size	0	0	0	68	41	42	21	0
Symptoms	0	0	0	47	6	4	2	0
Staging	-	-	-	-	2	-	-	30

Table 2.2 Hematological indications of splenectomy (Haematologica 1999; 84: 431-436)

	Number of cases
Chronic Idiopathic Thrombopenic Purpura	437
HIV Thrombocytopenia	33
Hereditary Spherocytocis	63
Hodgkin Disease (Staging)	59
Chronic Autoimmune Hemolytic Anemia	56
Non - Hodgkin lympoma	29
Chronic Lymphocytic Leykemia	16
Myeloproliferative syndromes - Myelofibrosis	11
Hairy Cell Leykemia	8
Sickle Cell Anemia	4
Beta thalassemia	2
Total	718

2.1.1 Idiopathic Thrombocytopenic Purpura

Idiopathic thrombocytopenic purpura is classified in acute and chronic. Presents with intense thrombocytopenia without known cause. In most cases upper respiratory tract infection has been preceded.

Acute form manifests in children mostly while chronic form affects female adults.

Antibodies against the membrane glycoprotein GPIIIb/IIa of the platelets are discovered in serum examination. Splenomegaly exists on 20% and the marrow is infiltrated by small hypolobated megakaryocytes.

Treatment of choice is the administration of steroids. In childhood thrombocytopenia subsides spontaneously and many researchers restrict their use in cases of hemorrhagic disorders.

If daily doses larger than 10 mg prednisone required in order to achieve platelets levels above 80 $x10^9$ or when during the staged withdraw of steroids there is relapse of the thrombocytopenia with hemorrhagic manifestations besides the use of immunoglobulin, then splenectomy is indicated. In 60% of the cases, platelet recover to normal levels without further treatment, while on 20% of the cases platelets number is below normal without hemorrhagic manifestations.Finally there are 20% of the cases that besides splenectomy, treatment is mandatory. In these cases phagocytosis of the platelets occurs in liver. Patients of extreme ages (elderly or below 7yo) are not candidates for splenectomy.

In case of relapse, immunosuppressive regiments are administered (azathioprime, cyclophosphamide). Platelet transfusions should be avoided because they promote the immune response.(12)

2.1.2 Hereditary Spherocytosis

Is a familial disease that is inherited as a dominant trait but in rare cases could be inherited as recessive. Clinical presentation includes anemia, jaundice, splenomegaly with production of red blood cells that are sphere-shaped. There's a wide range of clinical manifestations form light forms without symptoms to more serious life threatening forms (hemolytic, megaloblastic or aplastic crisis)

At first, the cause was thought to be the increased osmotic fragility of erythrocytes but later spleen's involvement was described. Many years after found that loss of sodium and lipids from erytrhocytes leads to abnormal cellular membrane. The present theory discusses the derangement of the cellular membrane's frame and malformation of its proteins. It remains the most common inherited hemolytic anemia in Northern Europe.

Two factors are responsible for its pathophysiology:

1. Intracellular erythrocyte abnormality
2. Participation of the spleen which sequestrates and destructs spherocytes.

Hemolytic anemia subsides after splenectomy but erythrocytes live less than normal. Indications of splenectomy are symptomatic hemolytic anemia, mild hemolytic anemia in

the presense of cholelithiasis and the history of chololithiasis among brothers. Failure following splenectomy is due to the presense of accessory spleen or the presence of second hemolytic condition like puruvate kinase deficiency. Splenectomy in children should be done after the 6th year in order to avoid the possibility of septicemia. (13)

2.1.3 Homozygous B – thalassemia

Beta thalassemias are a group of inherited blood disorders caused by reduced or absent synthesis of the beta chains of hemoglobin. Beta thalassemias are caused by point mutations at the b genomic complex and rarely from deletions on some parts of the DNA.

Homozygous beta thalassemia is diagnosed in the first years of life. Clinical presentation includes:

1. Paleness on the face and palms
2. Jaundice
3. Hepatosplenomegaly that repulses the lower thoracic ribs causing a chest deformity know as pectus carinatum (protruded chest)
4. Mongoloid face
5. Extramedullary hemopoiesis
6. Skin discoloration and venous ulcers at the tibia
7. Hormonal derangement like:

a. Pituitary Dwarfism
b. Hypogonadism
c. Hypoparathyroidism
d. Diabetes mellitus
e. Osteoporosis

Up to now, there's no cure. Patients should be transfused with compatible blood products, in order to avoid immune responses that reduce the lifetime of the transfused red blood cells. Erythropoiesis should be supported with administration of folic acid and excess iron should be removed with chelation therapy.

Bone marrow transplantation is indicated in children without cardiac or hepatic complications, with a promising outcome. Nowadays there is a lot of research on genetic therapy.

Indication for splenectomy is the presence of splenomegaly, especially when the need for transfused blood is 20 – 25% higher than the estimated needs (175ml of red blood cells/kg of body weight/yearly.

Because of the decreased immune response following splenectomy, it should be avoided in young ages. (14)

2.1.4 Sickle cell disease

Sickle-cell disease (**SCD**), or **sickle-cell anaemia** (**SCA**) or **drepanocytosis**, is a hereditary blood disorder, characterized by red blood cells that assume an abnormal, rigid, sickle shape because of the presence of hemoglobin S (HbS). Major clinical manifestations are chronic hemolytic anemia, vaso – occlusive crisis, chronic organ failure and predisposition for infections.

In sickle cell disease, spleen enlarges in the first year of life but afterwards undergoes atrophy because of the repeated infarcts. Spleen atrophy presents in 80 – 85% of patients with HbSS and in 50% of patients with HbS/β MA. Presence of high levels of HbF with coexisting homozygous a thalassemia reduce the frequency of vaso – occlusive strokes resulting in preservation of splenomegaly in adults.

Whether spleen remains enlarged the most possible complications are sequestration crisis, anemia, leykopenia, thrombocytopenia. In that case splenectomy is indicated. (15)

2.1.5 Autoimmune hemolytic anemia

Autoimmune hemolytic anemia (or autoimmune haemolytic anaemia; AIHA) occurs when antibodies directed against the person's own red blood cells (RBCs) cause them to burst. AIHA is classified as idiopathic or secondary in the coexistence of other disease or caused by drug administration. AIHA is classified according to the temperature attitude as either warm autoimmune hemolytic anemia or cold autoimmune hemolytic anemia, which includes cold agglutinin disease, and paroxysmal cold hemoglobinuria.

AIHA affects 1 people per 80.000 per year irrespective of age but with female predominance. Secondary AIHA is more frequent in people over 28 years old. Warm antibodies are produced in patients with neoplasmatic or infectious diseases. Also factors

like genetic predisposition or disorder of immune response also exist. Nevertheless the understanding of immune response, we know little about the origin of warm antibodies. One the other hand, in the case of cold antibodies, antigens are known.

The seriousness of clinical manifestations by warm antibodies varies from mild to lethal hemolysis. Symptoms include fatigue, jaundice, hemoglobinuria, dizziness, angina, dyspnea and fever.

Steroids are the first line of treatment in AIHA by suppressing the production of antibodies. Cytotoxic drugs like azathioprine or cyclophosphamide act in the same way.

Destruction of erythrocytes covered with IgG antibodies is due to adhesion to macrophages through FCR γ I – III receptors. Nonetheless, the fusion IgG – FCR has a low affinity and a lot of adhesions required for the erythrocyte to be destructed. Spleen is an ideal place for this to happen because erythrocytes remain there long enough to adhere with macrophages. Macrophages that manage to escape, have lost a part of their membrane thus becoming rounded and ultimately are sequestrated by the spleen. That's why splenectomy can improve the outcome in AIHA.

The administration of high doses of immunoglobulins takes advantage of the low affinity between IgG and FCR receptors. Nevertheless, their administration is not so effective in AIHA. Concluding, the sequence of therapeutic interventions in AIHA is by priority:

Steroids, cytotoxic drugs, IVIG, anti – CD20 and splenectomy.

In AIHA by cold antibodies, splenectomy is contraindicated because erythrocyte destruction happens in the liver.(16 – 18)

2.1.6 Lymphoproliferative syndromes

B-cell chronic lymphocytic leukemia (B-CLL), also known as chronic lymphoid leukemia (CLL), is the most common type of leykemia. Leukemias are cancers of the white blood cells (leukocytes). CLL affects B cell lymphocytes. B cells originate in the bone marrow, develop in the lymph nodes, and normally fight infection by producing antibodies. In CLL, B cells grow out of control and accumulate in the bone marrow and blood, where they crowd out healthy blood cells. CLL is a disease of adults, but, in rare cases, it can occur

in teenagers and occasionally in children (inherited). Most (>75%) people newly diagnosed with CLL are over the age of 50, and the majority are men.

Neoplasmatic lymphocyte is small in size with immature nucleus. In its surface presents B – cell antigens (CD19,CD20,CD21,CD22,CD23,CD79a) ,HLA – DR antigen and in 95% of the cases T – cell CD5 antigen.

Most people are diagnosed without symptoms as the result of a routine blood test that returns a high white blood cell count, but, as it advances, CLL results in swollen lymph nodes, spleen and liver, and eventually anemia and infections

Important factors in prognosis except from the stage (A,B,C, Binet classification, or O,I,II,III , Rai staging system) are :

1. Chromosomal mutations
2. Leykocytosis and splenomegaly without lymphadenopathy
3. Diffuse infiltration of the bone marrow
4. The presense of pre – lymphocytes in peripheral blood smear at 10%
5. The germination of lymphocytes in less than a year

Therapeytic intervention is indicated only in patients with:

1. bulky disease of stage C
2. lymphocytes > 100.000/ml
3. splenomegaly
4. known autoimmune cytopenias

Treatment is supportive and strictly anti – neoplasmatic.

Splenectomy is indicated only in symptomatic splenomegaly and hemolytic manifestations refractory to other treatments.(19)

B cell lymphoma

The term b – cell lymphoma is used for lymphomas that present the same histological and immunological characteristics of the B-cell chronic lymphocytic leukemia but at the time of diagnosis blood is not affected.

Treatment is the same as B-cell chronic lymphocytic leukemia

Splenic marginal zone lymphoma (SMZL) is a lymphoma made up of B-cells that replace the normal architecture of the white pulp of the spleen. The neoplastic cells are both small lymphocytes and larger, transformed blasts, and they invade the mantle zone of splenic follicles and erode the marginal zone, ultimately invading the red pulp of the

spleen. Bone marrow infiltration presents in 50% of the cases either focal or diffuse with various plasmatocytic differentiation. Immunophenotype includes slg+, HLA-, DR+,FMC7+, CD5- and CD10-. Antigens CD19,CD20,CD22 are expressed while CD21 & CD23 are not. Disease has a slow progression, can be treated with anti – D20 antibodies but the best results are achieved with splenectomy. (20,21)

Hairy cell leukemia is an uncommon hematological malignancy characterized by an accumulation of abnormal B lymphocytes

Hairy cell expresses surface IgG or IgA and positive phenotype of CD19,CD20,CD22,CD79a,FMC7 and HLA-DR. Antigens expressed are CD25 antigen of IL-2 receptor, CD11c , CD103 and IL-4 The disease affects men mostly and presents with pancytopenia, and enlargement of liver and spleen. Hepatosplenomegaly is due to infiltration by hairy cells. Bone marrow and immunological insufficiency progress over time. Initially treatment of HCL was splenectomy. Lately chemotherapeytic regimens are used, like cladribine (2CDA) and pentostatin (DCF) that manage to achieve remission without the need of splenectomy. Nowadays monoclonal antibody anti – CD20 has been introduced for the treatment of HCL (22)

2.1.7 Myeloproliferative diseases.

In this group are classified the idiopathic polycythemia, the chronic myeloid leykemia, the idiopathic thrombocytosis and myelofibrosis.

2.1.8 Myelofibrosis

Myelofibrosis, also known as myeloid metaplasia,chronic idiopathic myelofibrosis, osteomyelofibrosisand primary myelofibrosis is a disorder of the bone marrow. It is currently classified as a myeloproliferative disease in which the proliferation of an abnormal type of bone marrow stem cell results in fibrosis, or the replacement of the marrow with collagenous connective tissue fibers

Bone marrow fibrosis is reactive and accompanies the abnormal hyperplasia of megakaryocytes that secrete the Platelet Derived Growth Factor (PDGF) which activated fibroblasts while platelets secrete Platelets Factor 4 (PF4) that inactivates collagenase. In

that way fibroblastic activity is promoted in bone marrow while collagen production isn't limited.

The disease affects older adults mostly with major symptoms :

1. Abdominal fullness related to an enlarged spleen (splenomegaly).
2. Bone pain
3. Bruising and easy bleeding due to inadequate numbers of platelets
4. Fatigue
5. Increased susceptibility to infection, such as pneumonia or diarrhea
6. Pallor and shortness of breath while doing physical work due to anemia

Diagnostic

1. Primary myelofibrosis can begin with a blood picture suggestive of polycythemia vera or CML
2. Most patients have moderate to severe anemia
3. Eventually the patient develops thrombocytopenia
4. The peripheral smear appears markedly abnormal
5. Red cell abnormality includes bizarre shapes, (tear drop- shaped RBCs).
6. Nucleated erythroid precursors are seen in the peripheral blood
7. Immature white cells are also seen and basophils are increased
8. Teardrop shaped red blood cells on a peripheral smear

Prognosis

Myelofibrosis progresses in acute leykemia in 10 – 20% of the cases. Therapeytic interventions include:

1. Administration of alopourinol
2. Blood transfusions so that Hb remains 10g/dl
3. Administration of small doses of hydroxyurea
4. Radiation therapy in case of splenomegaly
5. Splenectomy in case of failure of treatment with hydroxyurea or radiation or in excessive thrombocytopenia. In the latter case splenectomy can be hazardous because removes a source of hemopoiesis while bone marrow is unable to produce blood products. Finally it should be noted that autologous bone marrow transplantation has been used in the treatment of myelofibrosis.(23)

2.1.9 Splenectomy – hypersplenism

The term hypersplenism is widely used indeterminably. Nowadays, hypersplenism is a syndrome in which splenomegaly is combined with reduction in the number of one or more blood cell type while bone marrow remains normal or hyperplastic.

Hematologic diseases that cause secondary hypersplenism are:

1. Blood neoplasms: Leykemias, lymphomas
2. Myelofibrosis and myeloproliferative diseases
3. Chronic hemolytic anemias: thalassemia, hemoglobinopathies
4. Myelodysplastic syndromes
5. Autoimmune hemolytic anemia
6. Autoimmune thrombocytopenia
7. Spleen hemangioma, hypo gamma globulinemia with hypersplenism

Indication of spleenectomy in hypersplenism incurs when clinical manifestations of anemia, leykopenia and thrombocytopenia are present.

Hypersplenism based only in laboratory findings is not an indication for splenectomy (24,25)

2.2 Laparoscopic Splenectomy

Laparoscopic splenectomy is the gold standard for managing patients with indication for spleen resection. (Figures 2.1 – 2.3) . (26) Determinative factor is the surgeon's experience given its infrequent use in addition to laparoscopic cholocystectomy. (26) Should be noted that there are no evidence from double blind randomized studies (Class I) that fill certain criteria about the superiority of the technique. Laparoscopic splenectomy has the classic advantages of less post procedural pain, shorter hospital stay, faster rehabilitation and better aesthetic result while being safe and efficient like open surgery. (26 – 28)

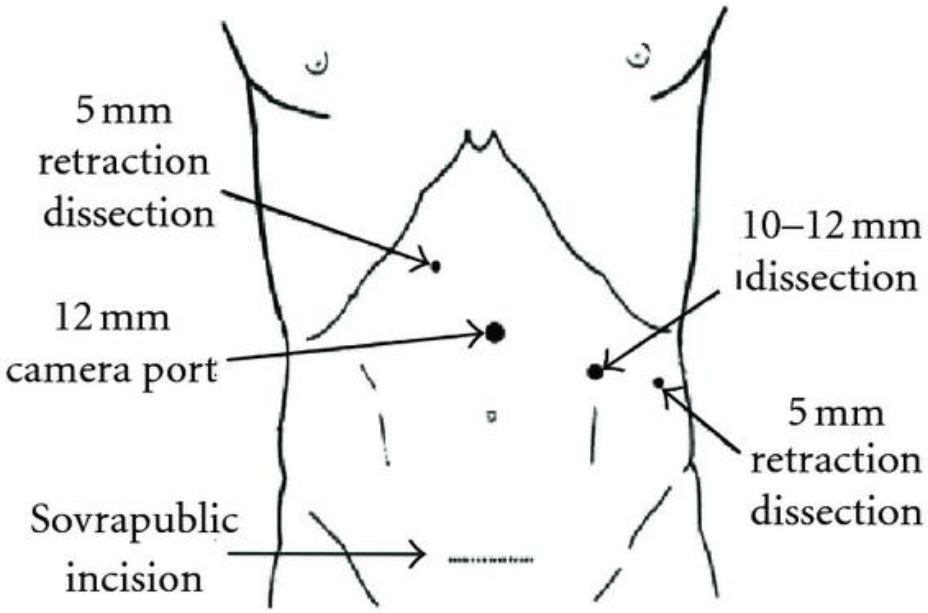

Figure 2.1 Trocar's placement in laparoscopic splenectomy

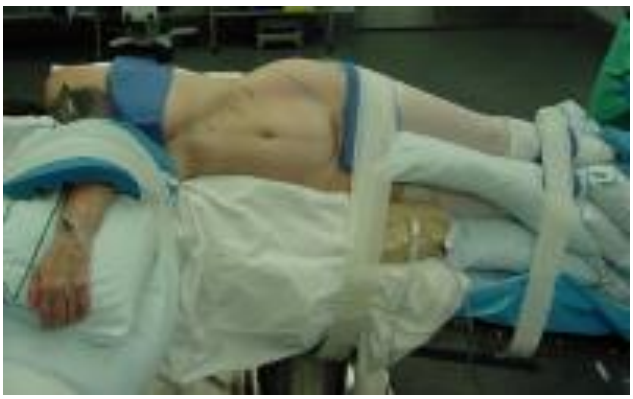

Figure 2.2 Patient's placement in laparoscopic splenectomy

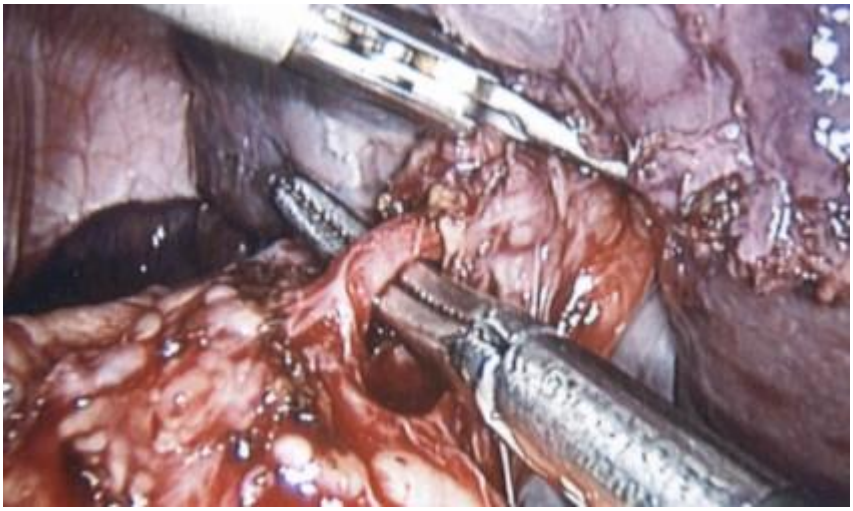

Figure 2.3 Laparoscopic splenectomy – Dissection of splenic artery

Indications for splenectomy are the same among laparoscopic and open surgery. Relative contraindications are like other laparoscopic interventions ,previous abdominal operations, coagulation disorders and especially in the case of spleen, the enlargement of hilar lymphnodes and the large size of the organ. Preoperative embolization of the splenic artery has been proposed for the reduction of the large size with the possible complication of pulmonary embolism.(26) Finally laparoscopic splenectomy can been used in case of traumatic rupture provided that the patient is hemodynamic ally stable. The later thechnique could be combined with preoperative embolization in order to control bleeding.

Worldwide bibliography as long as surgical practice in Greece support that laparoscopic spleenectomy is equally efficient as open surgical resection but lacks in the identification and the removal of accessory spleens.(26 – 29) Preoperative investigation of accessory spleens could facilitate the laparoscopic technique. (26) The need for transfusion as long as the operative duration is similar among the two techniques, after a

Hospital stay is less with laparoscopic technique, provided that surgical complications have been avoided. Laparoscopic technique has clear advantages over open surgery on postoperative pain, hospital stay and rehabilitation. The most important disadvantage is the duration of learning curve depending on the number of operations carried out by the surgeon preferably in experienced medical centers. (28)

PART TWO

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Aim

Splenectomy is a common surgical operation, with various indications. Depending on the indication of splenectomy, the procedure and its difficulty, as well as the postoperative outcomes may be different. Laparoscopic splenectomy was first reported by Rhodes et al (30) and since then has been widely used. (31-37)

The laparoscopic approach carries a smaller incidence of morbidity than open splenectomy and is feasible in most patients. (38) The natural orifice endoscopic approach, which is different than the laparoscopic approach, has no visible scar, but has been associated with increased complication rates, such as intra-abdominal organ injury. (36) It is also inferior in reproducibility, mainly due to the fact that the equipment that is needed is still not widely available. This equipment is very specific and has a long learning curve, whereas most surgeons are acquainted to laparoscopy equipment. Single Incision Laparoscopic Surgery (SILS) is a new variable of classic laparoscopic surgery, that uses the available laparoscopy equipment and demands just a few adjustments to the classic multiport laparoscopic technique. The SILS approach has so far been used in a variety of abdominal operations, such as cholecystectomy (39), appendectomy (40,41), colectomy (41) and thyroidectomy (42), and, recently, splenectomy. (43) Compared to conventional multiport laparoscopic surgery, SILS offers a better aesthetic outcome and reduced postoperative pain, while avoiding the possible complications from the trocar sites.

There is a limited number of studies available in the international literature on SILS splenectomy. The purpose of the present study is the review of the current literature on SILS splenectomy, and the analysis of the characteristics and outcomes of this novel technique. Also, we aim to investigate the advantages of SILS over conventional multiport laparoscopic surgery (MLS).

Materials and Methods

A systematic research of the medical literature published between 2009 and June 2013 was conducted, using PubMed, EMBASE and Google Scholar for publications on SILS splenectomy. The search was limited to English language publications. In order to avoid duplication of data, we only included articles from the same institution once if data

were being updated in a subsequent publication. The search terms were “single incision,” “single port,” “single access,” “single site,” “laparoscopic splenectomy,” “splenectomy,” and “laparoscopic splenic surgery.” All available publications from the review period were also considered.

Articles were selected if the abstract contained data of patients who underwent SILS-Sp for splenic diseases in the form of case reports, case series, and controlled or comparative studies. Conference abstracts were included if they contained relevant data. The reference lists of these articles were also reviewed to find additional candidate studies. In the case of duplicate publications, the latest and most complete study was included. Review articles were excluded from this study. Data extracted for this study were taken from the published reports; authors were not contacted to obtain additional information. The following data were collected from each eligible article: first author’s surname, publication date, study design, patient numbers, length of follow-up, main results, and conclusions. There was no limit on the minimum number of patients to include a study in our analysis. Case series were not reviewed if patient accrual was not consecutive. When multiple case series reported the same or a cumulative group of patients,only the most inclusive case series was selected. All articles selected for review of full text with the use of a standard form and a priori criteria for outcome assessments. Inclusion or exclusion was decided and the study data was abstracted. The flow chart of this selection process is summarized in Figure 1. The entire process of study selection, data analysis, and presentation of results was carried out in accordance with the Quality of Reporting Meta-Analysis (QUOROM) statement.

Complications related to splenectomy were defined as those occurring within 30 d of splenectomy or later if the complication occurred during the original hospitalization for splenectomy. Complications beyond the postoperative period thatmay be attributable to the absence of the spleen were not analyzed. All data were entered into a Microsoft Access(Redmond, WA) database. Morbidity rates with SILS-Sp and MLS were compared by using the chi-square test. A two-side $dP < 0.05$ was considered statistically significant.

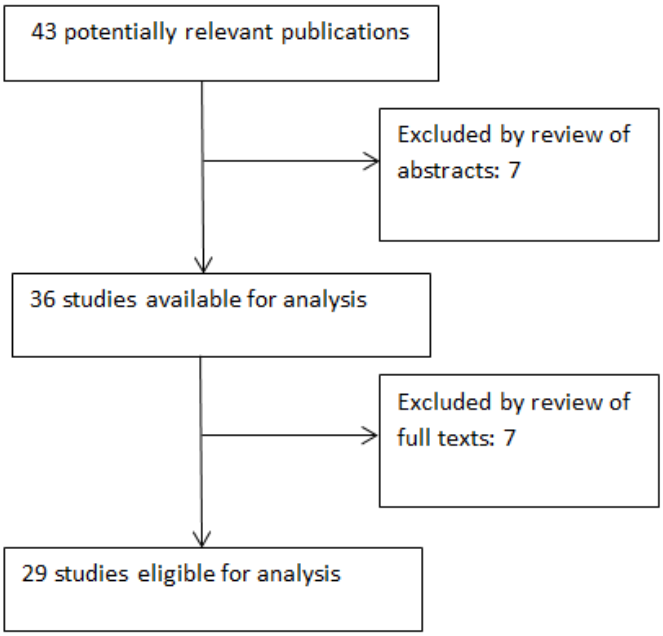

Figure 1.The flow chart of the selection process.

Results

Study characteristics

Using the aforementioned search strategy, we identified a total of 43 potentially relevant citations. four irrelevant articles and three non-English articles were excluded from review of titles and abstracts. Thirty-six publications were selected for review of full text and five duplicate publications and two review articles were excluded from further review. Twenty-nine studies[44-72], with a total of 105 patients undergoing SILS-Sp, met the criteria for analysis. These included four case-matched comparative studies (Table 1). There were no randomized controlled trials and meta-analyses.

Indication for surgery and procedure details

Indications for SILS-Splenectomy were varied in these series with the most common indication being idiopathic thrombocytopenia(n= 28, 26.7%), followed by splenic cystic disease(n = 14, 13.3%)and hereditary spherocytosis (n = 10, 9.5% (Table 2). Other less common indications included splenic tumor (n =5, 4.76%), liver cirrhosis, b-thalassemia, myeloproliferative disorder, hemolytic, and splenic aneurysm. Indications also included human immunodeficiency virus related hypersplenism, splenic abscess, splenic rupture, torsion, and sickle cell disease with one case in each indication. Indications for SILS-Splenectomy were not specified in 30 of patients.

The most common surgical procedures performed in the series were total splenectomy (n = 95, 90.48%) followed by splenic cyst unroofing (n=7, 6.67%), partial splenectomy(n = 2, 1.91%), and detorsion (n=1, 0.96%).Six studies described combined operations including cholecystectomy(n =8, 7.62%), mesh-pexy (n= 1, 0.96%), and pericardial devascularizaion (n =1, 0.96%).Fifteen studies used a commercially available single-port device for all or part of the cases (Table 3). Hong et al. [72] and Choi et al. [48] performed SILS-Splenectomy using a “custom” multichannel port device where each trocar was introduced intraperitoneally through each finger of a surgical glove attached to the wound retractor. Fifteen studies used conventional rigid ports for all or part of the cases placed through a single skin incision to perform the procedures.

All studies, except those by Lagrand and Kehdy [71], Vatansevand Ece [70], Taher and Tawfeeq [68], and Dapri et al. [50] used three trocars placed through the single access device or single skin incision. Fifteen studies reported on the type of laparoscopes used. All the studies except those by Saber and El-Ghazaly [66] and Boone et al. [46] reported using 30 degree-angled scopes. The types of instruments used are detailed in Table 3. The novel use of a Dominguez Magnetic Grasper to facilitate SILS Splenectomy was also reported.

The initial skin incision for insertion of the port systems measured 1-4 cm in 21 studies and the average length of the final scar was between 1.6 and4.5 cm in 10 studies.

Surgical outcomes

The surgical outcomes are summarized in Table 4. In 23 studies with available data, the man hospital stay was reported to be 1-11 days. 9 studies reported a mean length of stay

<3 days. The operative time for SILS splenectomy (including concurrent procedures) was 28-420 minutes in 27 of the studies. The estimated blood loss was 0-350 mL in 9 of the studies. From the 105 cases selected for this review, an additional port was inserted in 3 (2,9%), and there were two conversions to open and three conversions to multiport laparoscopic surgery. The overall conversion rate was 4,8%.

The causes of conversion were as follows: hemorrhage in the splenic artery as a result of failure to fire the stapler in one patient , perisplenic adherences and oozing of the diaphragm surface in one patient, large spleen with failure to reach the upper pole of the spleen in one patient, venous bleeding from the splenic hilum in one patient, and continuous oozing from the short gastric vessels that required blood transfusion in one patient [38]. In four studies with available data, the mean/median weight of the removed spleen was 131-1442 g.

There was no intraoperative death in none of the studies. The postoperative morbidity rate was between 0-33,3%. Four patients developed postoperative complications such as hemorrhage, and two of them underwent reoperation in order to control it. Budzynski et al. (47) reported a patient that complained of abdominal and shoulder pain after undergoing SILS splenectomy. Postoperative US revealed a fluid collection in the splenic bed with no apparent changes in the blood chemistry. The patient underwent re-laparoscopy using SILS, and the hematoma was drained. This patient had an uneventful postoperative course.

Choi et al. (48) reported a patient that developed shock on the 1st postoperative day. Laparotomy was performed and intraabdomina lbleeding from small vessels was noted in the splenic fossa. The bleeders were ligated, and 6 U of packed red blood cells were transfused. The patient was discharged on the 7th postoperative day.

Boone et al. (46) reported two patients with complications, with one patient developing a postoperative deep vein thrombosis and one patient requiring re intubation and intensive care unit care for severe epistaxis due to thrombocytopenia.

Comparative study of short – term outcomes of SILS-Splenectomy and MLS

Only four reports compared the outcomes of SILS Splenectomy and MLS. Choi et al. (48) compared 34 patients undergoing SILS-Splenectomy and 32 patients undergoing

MLS. Patients undergoing SILS had a markedly greater spleen size than patients undergoing MLS (SILS-Sp, 10.78 cm versus MLS, 9.62 cm; P= 0.031). Patients undergoing SILS also had a significantlyhigher blood loss than patients undergoing MLS (SILS, 206.25 mL versus MLS, 111.11 mL; P = 0.047).Furthermore, patients undergoing SILS had a markedly higher numeric pain rating scale score than patients undergoing MLS (SILS, 3.81 versus 4.56; P= 0.041).Patients undergoing SILS-Sp and MLS had comparable operation time, gas passing days, diet intake days, postoperative requirement for analgesics, and length of postoperative hospital stay.

Bell et al. (45) compared 11 patients undergoing SILS and MLS and reported reduced operative time for SILS as experience with the procedure accumulated, which became comparable with operative time for MLS. The median spleen weight was 218 g for patients undergoingSILSand120 g for patients undergoing MLS(P=0.109). There were no intraoperative or postoperative complications. The median visual analog scale (VAS) pain score (scale of 0-10) for the first 24 h following SILS was 2.6in comparison with 1.1for MLS. The mean dose of morphine sulfate in the first 24 h (at0.1 mg/kg per dose) was 5 mg for SILS and 7 mg for MLS. The mean length of hospital stay was 4 days in both groups. Given the small sample size, no analysis for statistical significance was performed.

Boone et al. (46) compared eight patients undergoing SILS and 18 patients undergoing MLS and reported that the median operative time was significantly higher in the MLS group (MLS, 172 versus SILS, 92.5 min; P = 0.003). The median blood loss did not significantly differ between the two groups (SILS, 150 versus MLS, 50 mL; P = 0.25). The percentage of patients requiring blood transfusions was similar between the groups. The median length of hospital stay was 4 days in each group. The complication rates were similar in both groups (SILS, 25% versus MLS, 28%). Patients undergoing SILS used a lower total dose of narcotic medication, but this did not reach statistical significance in this study

Recently, Monclova et al. (61) compared eight patients undergoing SILS, 15 patients undergoing MLS, and 10patients undergoing reduced port access splenectomy (RPAS).The operative time was significantly higher in patients undergoing MLS (MLS, 83 min versus SILS, 131 min, or RPAS, 81 min; P= 0.01). No conversion to open surgery was reported in any group, and there was difference in intra- or postoperative outcome. Furthermore, there was no difference in analgesic requirement among the three groups. Patients undergoing

MLS and SILS had higher body mass index scores than patients undergoing RPAS, and there was no difference in body mass index scores between patients undergoing MLS and RPAS.

. **Tables**

Table 1. List of cases included in the present analysis

HS = Hereditary Spherocytosis, ITP = Idiopathic Thrombopenic Porpura, NA = Not Available, SC = Splenic Cyst

First author / Ye	**Patient Num**	**Indication for Sur**	**Operation**	**Incision Length (initia**
Vatansev(2009)(7	1	ITP	Total Splenectomy	2.5 NA
Malladi(2009)(59	1	ITP	Total Splenectomy	2.5 (2.5)
Dutta(2009)(51)	6	SC(5), ITP(1)	Total Splenectomy + Cholecystectomy (2)	NA (NA)
Tam(2010)(69)	3	β-thalassemia	Total Splenectomy + Cholecystectomy	1-1.5 (NA)
Hong(2010)(72)	1	SC	Partial Splenectomy	2 (2)
Saber(2010)(66)	1	SC	Unroofing	2(2)
Rottman(2010)(65	1	Lymphoma	Total Splenectomy	1.2 (NA)
Hansen(2010)(56)	1	SC	Total Splenectomy	2(2)
Lagrand(2010)(71	1	ITP	Total Splenectomy	NA (NA)
Barbaros(2010)(4	10	ITP	Total Splenectomyή	NA (NA)
Monclova(2012)(	8	Cancer(3), ITP(1), HIV-hypersplenism SC(1), SC(2)	Unroofing (2) Total Splenectomy(6)	1.5 -2 (NA)
Podolsky(2010)(6	2	NA	Total Splenectomy	1.8 – 2.5(4.5)
Taher(2011)(68)	1	ITP	Total Splenectomy	2 (NA)
Joshi(2011)(58)	1	Spleen abscess	Total Splenectomy	3 (NA)
Srikanth(2011)(67	1	ITP	Total Splenectomy	2 (NA)
Misawa(2011)(60	10	ITP(3), Cirrhosis (2), Splenic aneurysm(2 SC(1),Epithelial cy Spleen tumor (1)	Total Splenectomy	2 (NA)

Dapri(2011)(50)	1	ITP	Total Splenectomy	NA (1.6)
Colon(2011)(49)	2	ITP, Sickle cell anemia	Total Splenectomy + Cholecystectomy (1)	2 (2)
Fan(2011)(53)	1	Spleen rupture	Total Splenectomy	2 (2)
Budzynski(2011)(	3	ITP(2), SC(1)	Total Splenectomy	2.5 – 3 (NA)
Ergun(2011)(52)	5	SC(4), NA(1)	Unroofing (4) Total Splenectomy(1)	2 (2)
Garrett(2011)(55)	7	HS(3), ITP(1), Epidermoid cyst(1) Συστροφή(1) SC(1)	Total Splenectomy(5) + cholecystectomy (1) Mesh placement (1)	NA (NA)
Garey(2011)(54)	3	NA	Total Splenectomy+ Cholecystectomy	NA (NA)
Padilla(2011)(63)	1	NA	Total Splenectomy	NA (NA)
Oyama(2011)(62)	1	ITP	Total Splenectomy	2.5 (NA)
Jing(2012)(57)	1	Portal Hypertensior	Total Splenectomy+ Pericardial Devascular	2 -3 (NA)
Choi(2012)(48)	16	NA	Total Splenectomy	3 (3)
Bell(2012)(45)	7	SC	Total Splenectomy	2 (NA)
Boone(2012)(46)	8	MPD(3), ITP (2), Hemolytic Anemia SC (1)	Total Splenectomy+ N	4 (NA)

Table 2. Indication for splenectomy in the patient sample

Indication	**Patient number**	**Rate (%)**
ITP	28	26,7
Spleen cyst	14	13,3
Hereditary Spherocytosis	10	9,5
Spleen tumor	5	4,76
Hepatic cirrhosis	3	2,86
β-thalassemia	3	2,86
MDS	3	2,86
Hemolytic anemia	2	1,91
Spleen Aneurysm	2	1,91
Other	5	4,76
Not available	30	28,5
Total	105	100

Table 3.SILS equipment**.**

Author	**Approach**	**Position**	**Port systemScope**						**Vessel ligation**
			Port diameter	**Trocars**	**Tip**	**Width**	**Angle**	**Forceps/ Grasper**	
Vatansev	Navel	Semi lateral	2 ports	2 trocars (10, 10)	Rigid	10	30	Straight	EndoLoop
Malladi	Subcostal	Lateral	SILS port	3 trocars (5,5,5/12)	Rigid	5	30	Curved	Clip
Dutta	Navel	Semilateral	3 ports	3 trocars (5,5,5/12)	NA	NA	NA	Articulate	Clip
Tam	Navel	Semilateral	3 ports	3 trocars (5,5,5)	Rigid	5	30	Straight	LigaSure
Hong	Navel	Semi lateral	ALEXIS Wound Retractor + glove	3 trocars (5,5,10)	Rigid	10	30	Articulate	Clip
Saber	Navel	Semilateral	3 ports	3 trocars (5,5,10)	Rigid	10	45	Straight	NA
Rottman	Navel	Semi lateral	3 ports	3 trocars (5,5,5/12)	Rigid	5	30	Straight	Clip
Hansen	Navel	Semi lateral	3 ports	3 trocars (5,5,5/12)	Rigid	5	NA	Straight	Clip

Lagrand	Navel	Semi lateral	SILS port	NA	NA	NA	NA	Articulate	Clip
Barbados	Navel	Semi lateral	SILS port	3 trocars (5,5,5/15)	Rigid	5	30	Articulate	Clip
Monclova	Navel/ Subcostal	Semi lateral	3 ports Triport	3 trocars (5,5,12) 3 trocars (5,5,10)	Flexible	10	NA	Curved	Clip
Podolsky	Navel	Semi lateral	3 ports	3 trocars (5,5,5/12)	NA	5	NA	Straight	Clip
Taher	Navel	Semi lateral	SILS port	4 trocars (5,5,5,12)	Flexible/ NA	10/5	NA/30	Articulate	Clip
Joschi	Navel	Semi lateral	3 ports	3 trocars(5,5,10)	Rigid	10	NA	Straight	EndoLoop
Srikanth	Navel	Semi lateral	3 ports	3 trocars(5,5,10/12)	Rigid	10	NA	Articulate	Clip
Misawa	Navel	Semi lateral	SILS port	3 trocars(5,5,10/12)	Flexible	5	NA	Articulate	Clip
Dapri	Navel	Semi lateral	1 port	1 trocar (11)	Rigid	10	30	Curved	Clip
Colon	Navel	Semi lateral	3 ports	3 trocars (5,5,5/12)	Rigid	5	30	Straight	Clip
Fan	Navel	Semi lateral	3 ports	3 trocars (5,10,12)	Rigid	10	30	Straight	Clip
Budzynski	Navel	Semi lateral	SILS port	3 trocars (5,NA,NA)	Rigid	10	30	Articulate	NA
Ergun	Navel	Semi	SILS	NA	NA	NA	NA	NA	NA

		lateral	port						
Garrett	Navel	Semi lateral	SILS port	3 trocars (5,5,5)	Rigid	5	NA	Rotating	EndoLoop
Garey	Navel	Semi lateral	SILS port	NA	Rigid	NA	NA	Straight	NA
Padilla	Navel	Semi lateral	SILS port	NA	NA	NA	NA	NA	NA
Oyama	Left abdominal	Semi lateral	SILS port	3 trocars (5,5,5/12)	Rigid	5	NA	Rotating	Clip
Kong	Navel	Semi lateral	3 ports	3 trocars (5,10,12)	Rigid	10	30	Straight	Clip
Choi	Subcostal	Lateral	OCTOport/ Wound Retractor + glove	3 trocars (5,12,12)	Rigid	NA	NA	Straight	Clip
Bell	Navel	Semi lateral	3 ports/ Gelport/ Quadport	3 trocars (5,5,5/12)	Flexible	5	30	Rotating	Clip
Boone	Navel	Lateral	Gelport	3 trocars (10,10,10)	Rigid	10	45	NA	Clip

NA = Not available

Table 4. Surgical outcomes of SILS splenectomy

First Author/ Year	**OT (min)**	**EBL (m**	**CV (%)**	**AP (%)**	**PC (%)**	**RO (%)**	**POS (d)**	**SW (g)**
Vatansev(2009)(7	45	NA	0	0	0	0	1.5	NA
Malladi(2009)(59	133	NA	0	0	0	0	2	NA
Dutta(2009)(51)	90 (75-115)	NA	0	0	0	0	2.5	NA
Tam(2010)(69)	347 (300-420	NA	33.3 (1) toMLS	33.3 (1)	0	0	NA	NA
Hong(2010)(72)	145	NA	0	0	0	0	NA	NA
Saber(2010)(66)	87	NA	0	0	0	0	1	NA
Rottman(2010)(6	180	NA	0	0	0	0	3	NA
Hansen(2010)(56	84	NA	0	0	0	0	2	NA
Lagrand(2010)(71	NA	NA	0	0	0	0	1	NA
Barbaros(2010)(4	60-180	50-200	10 (1), To open	0	0	0	2-5	NA
Monclova(2012)(	97 (60-150)	NA	25 (2), toMLS	0	0	0	4(2-5)	485 (340-590
Podolsky(2010)(6	191	250	0	0	0	0	2-4	NA
Taher(2011)(68)	180	NA	0	0	0	0	3	NA
Joshi(2011)(58)	NA	NA	0	0	0	0	4	NA
Srikanth(2011)(67	150	NA	0	0	0	0	NA	NA
Misawa(2011)(60	230 (150-378	15 (0-100)	10 (1) toopen	10 (1)	0	0	6.8±2.3	260 (100-580
Dapri(2011)(50)	160	NA	0	0	0	0	3	NA
Colon(2011)(49)	160,216	NA	0	0	0	0	2	NA
Fan(2011)(53)	110	90	0	0	0	0	8	NA
Budzynski(2011)(	93	NA	0	0	33.3 (1)	33.3 (1)	NA	NA
Ergun(2011)(52)	48(28-64 and 200	NA	0	0	0	0	1.5(1-2) and 3	NA

Garrett(2011)(55)	136 (96-180)	30 (0-100)	0	14.3 (1)	0	0	3.2 (1-8)	NA
Garey(2011)(54)	90 ± 6 And 116	NA	0	0	0	0	1.5 and 1	NA
Padilla(2011)(63)	150	NA	0	0	0	0	NA	NA
Oyama(2011)(62)	123	1	0	0	0	0	4	NA
Jing(2012)(57)	240	350	0	0	0	0	NA	NA
Choi(2012)(48)	96.06±32	206.25± 142.45	0	0	6.25 (1)	6.25 (1)	5.13±1.6	NA
Bell(2012)(45)	138 (95-167)	NA	0	0	0	0	4.9 (3 - 9)	218 (130-316
Boone(2012)(46)	92.5 (79 – 175	50 (25-200)	0	0	25(2)	0	4 (2 - 11)	268.5 (131-144

AP = Additionalport, CV= Conversion, NA = No available, OT = Operative time, PC= Postoperative Complications, RO = Reoperation, SW = Spleen Weight

Discussion

The induction of laparoscopic surgery in the beginning of 1990s brought the surgical therapy of human disease in a whole new era. Less invasive techniques, such as Single Incision Laparoscopic Surgery, have been used in the surgery of the spleen since as early as 2009, when Barbados and Dincag (41) first reported the operation. In theory, the more the incisions and trocar sites during surgery, the greater the risk for abdominal wall hernias and wound infections. SILS splenectomy could probably reduce these complications. In contrast, the incision length during SILS splenectomy is mostly dependent to the size of the spleen, which is very big in case of spleen tumors that demand a histologic analysis of the whole sample. In fact, our analysis reveals that the size of the final incision was bigger than that of the initial incision in most cases, showing that the analysis on the cosmetic benefit of SILS splenectomy should be based on the final incision size and not the initial, or be based in objective cosmetic criteria.

Based on the literatures in this review, SILS-Splenectomy is indicated in patients withhematological disorders, including idiopathic thrombocytopeniapurpura, thalassemia, hairy cell leukemia, lymphoma,myelofibrosis, or hereditary spherocytosis; patientswith benignoccupying lesion, including splenic hemangioma and spleniccyst, and some patients with portal hypertension requiringsplenectomy. Patients with severe cardiorespiratory dysfunction,severe refractory coagulopathy,morbidobesity,pregnancy,andmegalosplenia (>30 cm in diameter) are contraindicated for SILS splenectomy.

Various operative parameters including operative time and blood loss are generally acceptable in this review. In particular, therate of conversion to open procedure (1.9%) is acceptable inthese series of SILS-Sp. This is partly because many SILS-Splenectomy cases could avoid laparotomy by adding additional ports asnecessary. This may lead to avoidance of negative outcomesassociated with open conversions. (73) Another possiblereason is that SILS-Sp has been done for selected patients byexperienced laparoscopic surgeons, which might lead to biasin the current analysis. Because most of the reports did notmention the details of the operators, we should be cautiousabout directly comparing these values to historical controls.

The overall mortality (0%) and morbidity (2,1%) rates in these series of SILS splenectomy is generally acceptableThe average/median length ofhospital stay varied from 1

to 11 d across reports. Comparativestudies reported that there were no significant differencesbetween the groups in average length of hospital stay. Studiescomparing postoperative median pain score between patientsundergoing SILS-Splenectomy and conventional laparoscopic surgery are still limited with conflictingresults. Our studies in other SILS procedures found that SlLSshowed a trend toward more severe incisional pain (74), whichmight be explained by the close placement of trocars ina confined space and stress exerted on the tissue by surgicalinstruments and laparoscope during the procedure.

With any new technology, associated cost needs to beconsidered. Unfortunately, no comparative studies were foundin this review. Because SILS-Splenectomy procedure requires purchasingaccess devices and additional equipment in somecases, demonstration of any economic benefit over MLS can bedifficult. Only fewer conversions, a shorter postoperativerecovery or length of hospital stay, and less morbidity willmake SILS-Splenectomy more cost-effective, which is still to be validated. Seventeen studies in thisreview used conventional or homemade instruments duringthe procedure, which will not increase the economic burden ofthe patients in port device itself.

It is obvious that SILS has several disadvantagescompared with multiport laparoscopic surgery as far as surgical instruments and techniques are concerned. Although SILS-Splenectomy can beperformed with a conventional rigid laparoscope and straightinstruments, crowding over the access port or access siteusually leads to clashing of surgical instruments. The parallelarrangement of instruments and the constant interferencebetween the surgeon and the camera operator, both add thedifficulty to the procedure. Furthermore, lack of triangulationsignificantly the difficulty of splenic exposureand dissection. In an attempt to improve surgical exposure,most surgeons used 30 degrees laparoscopes.Someauthors chose to use longer laparoscopes in order to avoid crowding in the field of the operation (47). Meanwhile, gastric suture and retraction of the stomach is also proposed by a few authors in order to better visualize the spleen during the operation (49, 60, 67).One of the most challenging factors for SILS-Splenectomy inattaining widespread use is the additional learning curverequired for this technique and there is concern for increasedcomplications resulting from surgeons who are less experiencedin laparoscopic surgery trying to adopt this technique.

Finally, investigating the present study’s limitations, it is obvious that the statistical analyses presented herein mostly depend on case reports and case series with significant

heterogeneity between them. It is therefore evident that the lack of uniform reporting on SILS splenectomy, as well as the variability of the techniques and approaches used do not allow for objective conclusions regarding the benefits and drawbacks of this novel technique.

Conclusions

In conclusion, according to the results of the present study, the early experience on SILS splenectomy show that it is a feasible and safe technique in the hands of the experienced laparoscopic surgeon. However, as it is an emerging technique, the lack of published data has to be an important factor that needs to be considered before we draw objective conclusions. The possible benefit of SILS splenectomy compared to conventional laparoscopic surgery has yet to be proved. Unfortunately, most reports are case series or case reports, and future multicentric randomized studies are necessary in order to better define the benefits of this new method compared to traditional multiport laparoscopic surgery.

ABSTRACT

Purpose: The scope of the present review is to assess the safety and possible benefit of single incision laparoscopic splenectomy (SILS-Sp)

Material and Methods: A systematic review of the published literature from 2009 to 2013 was performed.

Results: 29 studies that included 105 patients who underwent SILS-Sp were reviewed. In six of the studies, a concurrent operation was performed, including cholecystectomy (n=9), mesh application (n-1), and pericardial devascularization (n=1). The operative time range was 28-240 min and blood loss 0-350mL. From the 105 patients treated, an additional port was used in three cases. In three cases the operation was converted to multiport laparoscopic splenectomy, while in two it was converted to open splenectomy. Postoperative hemorrhage occurred in two patients, who required reintervention. Total mortality was 0% and the postoperative hospital stay was 1-11 days. Among the four published comparative studies, one showed bigger blood loss and lower postoperative pain in the SILS-Sp group versus conventional laparoscopy. Another study showed that SILS-Sp was less time-consuming (92,5 versus 172 min), and was associated with equal postoperative stay, reduced morbidity, equivalent mortality and comparable postoperative pain requiring analgesics.

Conclusions: In the early studies presenting carefully selected patient series, SILS-Sp seems to be a feasible and safe operation, when executed by experienced surgeons. Although, as an emerging technique, the lack of large-scale published series does not allow for solid conclusions.

ΠΕΡΙΛΗΨΗ

Σκοπός: Σκοπό αυτής της ανασκόπησης αποτέλεσε η εκτίμηση της ασφάλειας και τα πιθανά οφέλη μιας λαπαροσκοπικής σπληνεκτομής με μια οπή (SILS-Sp).

Υλικό - Μέθοδοι: Πραγματοποιήθηκε μια συστηματική ανασκόπηση της βιβλιογραφίας από το 2009 ως το 2013 με σκοπό την ανάλυση της σχετικής βιβλιογραφίας.

Αποτελέσματα: Έγινε ανασκόπηση ενός συνόλου 29 μελετών με 105 ασθενείς που υποβλήθηκαν σε SILS-Sp. Σε έξι μελέτες περιγράφηκαν συνδυαστικές επεμβάσεις περιλαμβάνοντας χολοκυστεκτομή (n=8), τοποθέτηση πλέγματος (n=1), και περικαρδιακή απαγγείωση (n=1). Το εύρος του χρόνου των επεμβάσεων και η εκτιμώμενη ποσότητα απώλειας αίματος ήταν 28 - 240 λεπτά και 0 - 350mL, αντίστοιχα. Από τους 105 ασθενείς, οι τρεις (2.9%) χρειάστηκαν επιπρόσθετο αυλό, σε δυο ασθενείς (1.9%) η επέμβαση μετατράπηκε σε ανοιχτή σπληνεκτομή και σε τρεις ασθενείς (2.9%) σε συμβατική πολυαυλική λαπαροσκοπική σπληνεκτομή (συνολικό ποσοστό μετατροπής, 4.8%). Μετεγχειρητική αιμορραγία συνέβη σε δυο ασθενείς (1.9%) οι οποίοι και οι δυο χρειάστηκαν επανεπέμβαση. Η συνολική θνησιμότητα ήταν 0% (0/105). Η διάρκεια της μετεγχειρητικής νοσηλείας ήταν μεταξύ 1-11 ημέρες. Ανάμεσα σε τέσσερις δημοσιευμένες συγκριτικές μελέτες, μια έδειξε μεγαλύτερη εκτιμώμενη απώλεια αίματος και χαμηλότερο αριθμητικά μετρούμενο πόνο στην ομάδα της SILS-Sp σε σχέση με την ομάδα με την πολυαυλική λαπαροσκοπική σπληνεκτομή. Μια άλλη συγκριτική μελέτη έδειξε ότι η SILS-Sp σχετιζόταν με μικρότερο διεγχειρητικό χρόνο (92.5 έναντι 172 λεπτά), ίση διάρκεια νοσηλείας στο νοσοκομείο, μειωμένο ποσοστό επιπλοκών, παρόμοια θνητότητα και συγκρίσιμες μετεγχειρητικές απαιτήσεις σε ναρκωτικά αναλγητικά.

Συμπεράσματα: Σε πρώιμες σειρές ασθενών με αυστηρή επιλογή, η SILS-Sp φαίνεται να είναι πραγματοποιήσιμη και ασφαλής όταν διενεργείται από έμπειρους λαπαροσκόπους χειρουργούς. Ωστόσο, ως αναδυόμενη επέμβαση, η έλλειψη μεγάλων δημοσιευμένων σειρών θα πρέπει να είναι ένας παράγοντας που θα πρέπει να ληφθεί υπόψη πριν μπορέσουμε να καταλήξουμε σε αντικειμενικό συμπέρασμα.

References

1. Gray H. Gray's Anatomy. 35 ed. Wacwick R, Williams PL, editors. Edinburgh: Longman.

2. Seufert R, Mitrou P. Surgery of the Spleen. New York: Thieme Verlag; 1986.

3. Crosby W. The spleen. NewYork: McGrawHill; 1980.

4. Τσούρας Σ. Μαθήματα Ιστολογίας του Ανθρώπου1976.

5. Kahle W, Leonhardt H, Platzer W. Taschenatlaw der Anatomie. Innere Organe. Stuttgart: Georg Thieme Verlag; 1984.

6. Chen LT. Microcirculation of the spleen: and open or closed circulation? Science1978 Jul 14;201(4351):157-9.

7. Amsbaugh DF, Prescott B, Baker PJ. Effect of splenectomy on the expression of regulatory T cell activity. J Immunol1978 Oct;121(4):1483-5.

8. Lennert K, Stutte M, editors. Stoff wechsel und Membran-Permabilitat von Erythrozyten und Thrombozyten.1 Internat Symposium; 1968; Stuttgart.

9. Arnoletti JP, Karam J, Brodsky J. Early postoperative complications of splenectomy for hematologic disease. Am J Clin Oncol1999 Apr;22(2):114-8.

10. Baccarani U, Donini A, Terrosu G, Pasqualucci A, Bresadola F. Laparoscopic splenectomy for haematological diseases: review of current concepts and opinions. Eur J Surg1999 Oct;165(10):917-23.

11. Baccarani U, Terrosu G, Donini A, Zaja F, Bresadola F, Baccarani M. Splenectomy in hematology. Current practice and new perspectives. Haematologica1999 May;84(5):431-6.

12. Diagnosis and treatment of idiopathic thrombocytopenic purpura: recommendations of the American Society of Hematology. The American Society of Hematology ITP Practice Guideline Panel. Ann Intern Med1997 Feb 15;126(4):319-26.

13. Hassoun H, Palek J. Hereditary spherocytosis: a review of the clinical and molecular aspects of the disease. Blood Rev1996 Sep;10(3):129-47.

14. Lucarelli G, Giardini C, Angelucci E. Bone marrow transplantation in thalassemia. Cancer Treat Res1997;77:305-15.

15. Higgs DR, Aldridge BE, Lamb J, Clegg JB, Weatherall DJ, Hayes RJ, et al. The interaction of alpha-thalassemia and homozygous sickle-cell disease. N Engl J Med1982 Jun 17;306(24):1441-6.

16. Schreiber AD. Clinical immunology of the corticosteroids. Prog Clin Immunol1977;3:103-14.

17. Pirofsky B. Hereditary aspects of autoimmune hemolytic anemia; a retrospective analysis. Vox Sang1968;14(5):334-47.

18. Schwartz SI, Bernard RP, Adams JT, Bauman AW. Splenectomy for hematologic disorders. Arch Surg1970 Aug;101(2):338-47.

19. Mentzer SJ, Osteen RT, Starnes HF, Moloney WC, Rosenthal D, Canellos G, et al. Splenic enlargement and hyperfunction as indications for splenectomy in chronic leukemia. Ann Surg1987 Jan;205(1):13-7.

20. Morel P, Dupriez B, Gosselin B, Fenaux P, Estienne MH, Facon T, et al. Role of early splenectomy in malignant lymphomas with prominent splenic involvement (primary lymphomas of the spleen). A study of 59 cases. Cancer1993 Jan 1;71(1):207-15.

21. Ahmann DL, Kiely JM, Harrison EG, Jr., Payne WS. Malignant lymphoma of the spleen. A review of 49 cases in which the diagnosis was made at splenectomy. Cancer1966 Apr;19(4):461-9.

22. Bouroncle BA. Thirty-five years in the progress of hairy cell leukemia. Leuk Lymphoma1994;14 Suppl 1:1-12.

23. Barosi G, Ambrosetti A, Centra A, Falcone A, Finelli C, Foa P, et al. Splenectomy and risk of blast transformation in myelofibrosis with myeloid metaplasia. Italian Cooperative Study Group on Myeloid with Myeloid Metaplasia. Blood1998 May 15;91(10):3630-6.

24. Coon WW. Splenectomy for thrombocytopenia due to secondary hypersplenism. Arch Surg1988 Mar;123(3):369-71.

25. Coon WW. Splenectomy for cytopenias associated with systemic lupus erythematosus. Am J Surg1988 Mar;155(3):391-4.

26. Feldman LS. Laparoscopic splenectomy: standardized approach. World J Surg2011 Jul;35(7):1487-95.

27. Borie F, Philippe C. [Laparoscopic splenectomy: indications, techniques, outcomes]. J Chir (Paris)2009 Aug;146(4):336-46.

28. Cai YQ, Zhou J, Chen XD, Wang YC, Wu Z, Peng B. Laparoscopic splenectomy is an effective and safe intervention for hypersplenism secondary to liver cirrhosis. Surg Endosc2011 Dec;25(12):3791-7.

29. Laopodis V, Kritikos E, Rizzoti L, Stefanidis P, Klonaris P, Tzardis P. Laparoscopic splenectomy in beta-thalassemia major patients. Advantages and disadvantages. Surg Endosc1998 Jul;12(7):944-7.

30. Rhodes M, Rudd M, O'Rourke N, Nathanson L, Fielding G. Laparoscopic splenectomy and lymph node biopsy for hematologic disorders. Ann Surg1995 Jul;222(1):43-6.

31. Bresler L, Guerci A, Brunaud L, Ayav A, Sebbag H, Tortuyaux JM, et al. Laparoscopic splenectomy for idiopathic thrombocytopenic purpura: outcome and long-term results. World J Surg2002 Jan;26(1):111-4.

32. Carobbi A, Romagnani F, Antonelli G, Bianchini M. Laparoscopic splenectomy for severe blunt trauma: initial experience of ten consecutive cases with a fast hemostatic technique. Surg Endosc2010 Jun;24(6):1325-30.

33. Chowbey PK, Goel A, Panse R, Sharma A, Khullar R, Soni V, et al. Laparoscopic splenectomy for hematologic disorders: experience with the first fifty patients. J Laparoendosc Adv Surg Tech A2005 Feb;15(1):28-32.

34. Kye BH, Park IS, Kim JG, Lee JC, Son GM, Suh YJ, et al. Laparoscopic splenectomy: 3 ports are enough. Surg Laparosc Endosc Percutan Tech2010 Apr;20(2):104-8.

35. Pattenden CJ, Mann CD, Metcalfe MS, Dyer M, Lloyd DM. Laparoscopic splenectomy: a personal series of 140 consecutive cases. Ann R Coll Surg Engl2010 Jul;92(5):398-402.

36. Sotomayor-Ramirez RK. Efficacy and safety of laparoscopic splenectomy: review of 14 adult cases using the lateral approach. Bol Asoc Med P R2009 Apr-Jun;101(2):43-9.

37. Wang Y, Zhan X, Zhu Y, Xie Z, Zhu J, Ye Z. Laparoscopic splenectomy in portal hypertension: a single-surgeon 13-year experience. Surg Endosc2010 May;24(5):1164-9.

38. Maurus CF, Schafer M, Muller MK, Clavien PA, Weber M. Laparoscopic versus open splenectomy for nontraumatic diseases. World J Surg2008 Nov;32(11):2444-9.

39. Wu SD, Han JY, Tian Y. Single-incision laparoscopic cholecystectomy versus conventional laparoscopic cholecystectomy: a retrospective comparative study. J Laparoendosc Adv Surg Tech A2011 Jan-Feb;21(1):25-8.

40. Amos SE, Shuo-Dong W, Fan Y, Tian Y, Chen CC. Single-incision versus conventional three-incision laparoscopic appendectomy: a single centre experience. Surg Today2012 Jun;42(6):542-6.

41. Gash KJ, Goede AC, Chambers W, Greenslade GL, Dixon AR. Laparoendoscopic single-site surgery is feasible in complex colorectal resections and could enable day case colectomy. Surg Endosc2011 Mar;25(3):835-40.

42. Fan Y, Wu SD, Kong J. Single-port access transaxillary totally endoscopic thyroidectomy: a new approach for minimally invasive thyroid operation. J Laparoendosc Adv Surg Tech A Apr;21(3):243-7.

43. Barbaros U, Dinccag A. Single incision laparoscopic splenectomy: the first two cases. J Gastrointest Surg2009 Aug;13(8):1520-3.

44. Barbaros U, Sumer A, Tunca F, Gozkun O, Demirel T, Bilge O, et al. Our early experiences with single-incision laparoscopic surgery: the first 32 patients. Surg Laparosc Endosc Percutan Tech2010 Oct;20(5):306-11.

45. Bell R, Boswell T, Hui T, Su W. Single-incision laparoscopic splenectomy in children. J Pediatr Surg2012 May;47(5):898-903.

46. Boone BA, Wagner P, Ganchuk E, Evans L, Evans S, Zeh HJ, et al. Single-incision laparoscopic splenectomy: preliminary experience in consecutive patients and comparison to standard laparoscopic splenectomy. Surg Endosc2013 Feb;27(2):587-92.

47. Budzynski A, Matlok M, Pedziwiatr M, Budzynski P, Tusinski M, Zub-Pokrowiecka A, et al. SILS (single incision laparoscopic surgery) - new surgical approach to peritoneal cavity. Adv Med Sci2011;56(1):18-24.

48. Choi KK, Kim MJ, Park H, Choi DW, Choi SH, Heo JS. Single-incision laparoscopic splenectomy versus conventional multiport laparoscopic splenectomy: a retrospective comparison of outcomes. Surg Innov2013 Feb;20(1):40-5.

49. Colon MJ, Telem D, Chan E, Midulla P, Divino C, Chin EH. Laparoendoscopic single site (LESS) splenectomy with a conventional laparoscope and instruments. JSLS2011 Jul-Sep;15(3):384-6.

50. Dapri G, Bron D, Himpens J, Casali L, Carnevali P, Koustas P, et al. Single-access transumbilical laparoscopic splenectomy using curved reusable instruments. Surg Endosc2011 Oct;25(10):3419-22.

51. Dutta S. Early experience with single incision laparoscopic surgery: eliminating the scar from abdominal operations. J Pediatr Surg2009 Sep;44(9):1741-5.

52. Ergun O, Tiryaki S, Celik A. Single center experience in single-incision laparoscopic surgery in children in Turkey. J Pediatr Surg2011 Apr;46(4):704-7.

53. Fan Y, Wu SD, Siwo EA. Emergency transumbilical single-incision laparoscopic splenectomy for the treatment of traumatic rupture of the spleen: report of the first case and literature review. Surg Innov2011

Jun;18(2):185-8.

54. Garey CL, Laituri CA, Ostlie DJ, Snyder CL, Andrews WS, Holcomb GW, 3rd, et al. Single-incision laparoscopic surgery in children: initial single-center experience. J Pediatr Surg2011 May;46(5):904-7.

55. Garrett D, Emami C, Anselmo DM, Torres MB, Nguyen N. Single-incision laparoscopic approach to management of splenic pathology in children: an early experience. J Laparoendosc Adv Surg Tech A2011 Dec;21(10):965-7.

56. Hansen EN, Muensterer OJ. Single incision laparoscopic splenectomy in a 5-year-old with hereditary spherocytosis. JSLS2010 Apr-Jun;14(2):286-8.

57. Jing K, Shuo-Dong W, Ying F. Transumbilical Single-Incision Laparoscopy Surgery Splenectomy Plus Pericaudial Devascularization in One Case With Portal Hypertension: The First Report. Surg Innov2012 Jan 5.

58. Joshi M, Kurhade S, Peethambaram MS, Kalghatgi S, Narsimhan M, Ardhanari R. Single-incision laparoscopic splenectomy. J Minim Access Surg2011 Jan;7(1):65-7.

59. Malladi P, Hungness E, Nagle A. Single access laparoscopic splenectomy. JSLS2009 Oct-Dec;13(4):601-4.

60. Misawa T, Sakamoto T, Ito R, Shiba H, Gocho T, Wakiyama S, et al. Single-incision laparoscopic splenectomy using the "tug-exposure technique" in adults: results of ten initial cases. Surg Endosc2011 Oct;25(10):3222-7.

61. Monclova JL, Targarona EM, Vidal P, Peraza Y, Garcia F, Otero CR, et al. Single incision versus reduced port splenectomy--searching for the best alternative to conventional laparoscopic splenectomy. Surg Endosc2013 Mar;27(3):895-902.

62. Oyama K, Sasaki A, Chiba T, Nitta H, Otsuka K, Wakabayashi G. Single-incision laparoscopic splenectomy for idiopathic thrombocytopenic purpura: report of a case. Surg Today2011 Aug;41(8):1091-4.

63. Padilla BE, Dominguez G, Millan C, Martinez-Ferro M. The use of magnets with single-site umbilical laparoscopic surgery. Semin Pediatr Surg2011 Nov;20(4):224-31.

64. Podolsky ER, Curcillo PG, 2nd. Single port access (SPA) surgery--a 24-month experience. J Gastrointest Surg2010 May;14(5):759-67.

65. Rottman SJ, Podolsky ER, Kim E, Kern J, Curcillo PG, 2nd. Single port access (SPA) splenectomy. JSLS2010 Jan-Mar;14(1):48-52.

66. Saber AA, El-Ghazaly TH. Single-incision transumbilical laparoscopic splenic cyst unroofing: first reported case. Am Surg2010 May;76(5):509-11.

67. Srikanth G, Wasim MD, Sajjad A, Shetty N. Single-incision laparoscopic splenectomy with innovative gastric traction suture. J Minim Access Surg2011 Jan;7(1):68-70.

68. Taher R, Tawfeeq M. Single-port laparoscopic splenectomy for idiopathic thrombocytopenic purpura. Ann Saudi Med2011 Nov-Dec;31(6):655-6.

69. Tam YH, Lee KH, Sihoe JD, Chan KW, Cheung ST, Pang KK. Initial experience in children using conventional laparoscopic instruments in single-incision laparoscopic surgery. J Pediatr Surg2010 Dec;45(12):2381-5.

70. Vatansev C, Ece IJ. Single incision laparoscopic splenetomy with double port. Surg Laparosc Endosc Percutan Tech2009;19(e225).

71. Lagrand R, Kehdy F. Laparoendoscopic single site splenectomy. Am Surg2010;76(E158).

72. Hong T, Lee S, You Y, Kim J. Single-port Laparoscopic partial splenectomy: a case report. Surg Laparosc Endosc Percutan Tech2010;20(e164).

73. Swanson TW, Meneghetti AT, Sampath S, Connors JM, Panton ON. Hand-assisted laparoscopic splenectomy versus open splenectomy for massive splenomegaly: 20-year experience at a Canadian centre. Can J Surg Jun;54(3):189-93.

74. Tian Y, Wu SD, Chen YS, Chen CC. Transumbilical single-incision laparoscopic cholecystojejunostomy using conventional instruments: the first two cases. J Gastrointest Surg2010 Sep;14(9):1429-33.