



Cohort Study

Prognostic scoring system of laparoscopic splenectomy in children with benign hematological diseases, a retrospective cohort study

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ABSTRACT

Purpose: laparoscopic splenectomy (LS) gained popularity during the last years among pediatric surgeons. Benign hematological diseases represent the main indications of that procedure. There are some score systems of difficulty of the technique. Most of them are for adult patients. The aim is to develop a prognostic score system of LS in children with benign hematological diseases.

Methods: LS was performed in all children with benign hematological diseases. The children were operated in lateral decubitus position. The control of pedicle was achieved using bipolar sealing devices, polymer clips or endoscopic linear staplers. Preoperative, operative, and postoperative data were recorded and analyzed. Children were divided into two groups A and B according to the onset of complications.

Results: 137 successive children were operated. The mean age of patients was 8.7 (4–15) years. The main indications of LS were thalassemia, spherocytosis, idiopathic thrombocytopenic purpura (ITP), and sickle cell anemia (SCA). The mean length of splenic axis in thalassemia and spherocytosis cases was 15.6 ± 2.3 cm. The mean amount of estimated blood loss (EABL) was 149 ± 43.2 ml in group A while it was 185 ± 44.4 ml in group B. The mean operative time in group A was 75.5 ± 22.5 min while it was 89.2 ± 20.6 min in group B.

Conclusion: the development of prognostic score of LS in children with benign hematological diseases can predict children who are more susceptible for complications. It helps to minimize these complications and improve the outcome of LS.

1. Introduction

Laparoscopic splenectomy (LS) gained popularity since it has been described for the first-time during nineties of past century. It has become the “golden method” for splenectomy in all ages including children [1].

The main advantages of laparoscopic surgery are well presented in LS. Children who had LS had short hospital stay, lesser postoperative pain, earlier and more rapid tolerance of oral intake and better quality of life later [2,3].

Standardization of technique of LS takes place through years. There is some debate about securing splenic pedicle, technical complexity, and the suitable size of spleen for laparoscopy. The procedure needs excellent laparoscopic skills and well-equipped centers. There is still to some extent high conversion rate that reaches approximately 34%. However, conversion to conventional surgery is not considered failure of technique [4,5].

During the past years, several trials and reports were conducted to

define whom patient might have technical difficulty. Some authors assumed that pathology, gender, splenic weight, and age had major effect on difficulty of procedure. However, there are other factors that may affect operative and postoperative results. In addition, these score systems were mainly designed for adult patients [6,7].

This study was performed to establish a score system that may help to detect prognosis of LS in children with benign hematological disease.

2. Methods

2.1. After obtaining institutional approval of the ethical committee board (approval code 33872/6/20)

The trial was registered at Clinical trials gov under identifier NCT04763733. [Laparoscopic Splenectomy in Children - Full Text View - ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04763733).

A retrospective cohort study was performed for all children that had

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LS between 2007 and 2020. Data has been reported in line with the STROCSS criteria [8].

Children who had LS during the period between 2007 and 2012 were excluded from study. This was mainly applied to standardize technique and avoid any effects related to learning curve of pediatric surgical team. All children with benign hematological diseases were included in the current study. Malignant splenic conditions, traumatic cases or children that had previous partial splenectomy and require total splenectomy were excluded.

Preoperative abdominopelvic ultrasound was performed to document size of spleen and associated gall bladder stones in hemolytic anemia. Routine laboratory investigations and coagulation profile were obtained for every child.

2.2. Surgical procedure

LS was performed in right lateral decubitus position with an angle between side of child and table 60°. Three ports were used in all cases. An accessory port was used in extremely large spleens (more than 16 cm in long axis). Telescope 30° was used at the umbilical port. A working port was inserted midway between umbilicus and xyphoid process and another port was inserted in left midclavicular line. The accessory port was inserted in the left anterior axillary line if required. Pedicle control was achieved by either bipolar sealing devices (BSD), hem o lok clip or endoscopic straight linear stapler. Retrieval of spleen was either done through retrieval bag or Pfannesstiel incision in cases of huge spleen.

2.3. Statistical analysis

Statistical analysis was done using IBM SPSS V. 24 (IBM, NY, USA). A descriptive analysis was obtained for patients included in the study. Patients' characteristics were studied to identify candidate variables predictive of complication. These variables were used to develop a risk score using regression models. The score, and the best identified clinical cutoff point, underwent development, stability testing, and internal validation.

All patients were compared for differences in demographics, clinical variables using independent sample *t*-test or for continuous data, and χ^2 test for categorical data. Statistically significant continuous variables were operationalized into categorical variables based on clinically relevant cutoffs and retested for statistical significance.

2.4. Risk score model building

Variables were deemed eligible for inclusion in the initial stage of model building if they were.

- 1 statistically significant at the univariate level after operationalization,
- 2 found in the literature to be relevant, and
- 3 was deemed by the study team that the variables were common enough to be risk factors for complications.

Pearson correlation coefficient as applied to detect the relationship between risk score categories and different operative measures.

The Receiver Operating Characteristics (ROC) analysis was performed to examine the ability of the score for predicting the prognosis of LS in children. It was mainly used to estimate the ability of score to differentiate children with no, moderate or high risk.

To determine the cutoff points of different variables, ROC was constructed for preoperative and operative variables.

3. Results

This study included 137 successive children with benign hematological diseases who had LS. The median age of patients was 8.7 years

(4–15 years). The median body weight was 20.6 (12–33) kg. The main indications of LS were thalassemia, spherocytosis, idiopathic thrombocytopenic purpura (ITP), and sickle cell anemia (SCA). There were 83 females. The mean length of splenic axis in thalassemia and spherocytosis cases was 15.6 ± 2.3 cm. The mean length of splenic axis in sickle cell anemia cases was 12.4 ± 3.5 cm. The mean length of splenic axis in ITP cases was 10.2 ± 3.2 cm (Table 1).

To build their score, authors studied the factors that may affect the prognosis of LS in children. These factors were two preoperative factors and two operative factors. The preoperative factors were the type of benign hematological disease and the long axis of spleen. The two operative factors were the estimated amount of blood loss (EABL) in ml and the method used for pedicle control. The analyzed parameters in relation to these factors were the operative time in minutes, hospital stay in days, visceral injury mainly pancreatic injuries which could be detected by measuring the levels of amylase and lipase in IU/dl and other complications that may take place according to Dindo classifications. Accordingly, children were categorized into groups, A and B. Group A (n = 96) included cases that pass smooth with no or minimal operative or postoperative difficulties and group B (n = 41) included children that had some operative and post-operative difficulties.

3.1. Preoperative data

There were 32 children with ITP, 30 children with thalassemia, 20 children with spherocytosis, and 17 children with SCA in group A. In group B there 5 children diagnosed as ITP, 17 children with thalassemia, 12 children with spherocytosis, and 7 children with SCA. The mean long axis of spleen was 12.6 ± 3.7 cm and 14.2 ± 3.5 cm in both groups respectively (Table 1).

3.2. Operative data

The mean amount of estimated blood loss (EABL) was 149 ± 43.2 ml in group A while it was 185 ± 44.4 ml in group B. In group A pedicle was controlled by BSD in 41 cases, Hem-o-lok in 38 cases and linear endoscopic stapler in 17 cases. In group B pedicle was controlled by BSD in eight cases, hem-o-lok in 12 cases and endoscopic linear stapler in 21 cases. was used to control hilum in 41 cases. The mean operative time in

Table 1
Preoperative, operative variables.

Variables	Group A (n = 96)		Group B (n = 41)		P
Hematological disease					
ITP	32	36.4%	5	12.19%	0.007*
Thalassemia	30	27.3%	17	41.46%	
Spherocytosis	20	21.6%	12	29.26%	
Sickle cell anemia	14	14.8%	7	17.07%	
Splenic long axis					
mean ± s.d	12.6	± 3.7	14.2	± 3.5	0.014*
Range	7.0	– 20.0	7.0	– 21.0	
Estimated amount of Blood loss(ml)	142.9	± 43.2	185.5	± 44.4	0.012*
Mean ± SD					
Pedicle control					
- BSD	41	42.7%	8	19.5%	0.017*
- Hem-o- lok	38	39.5%	12	29.2%	
- Endoscopic linear stapler	17	17.7	21	51.2%	
Operative time	75.5	± 22.5	89.2	± 20.6	0.001*
Hospital stay (median in days) and range	1		4		0.001*
Pancreatic injury	1–3		3–5		
- Amylase (mean ± SD)	62.0	± 20.6	246.7	± 121.4	0.001*
- Lipase (mean ± SD)					
U/I					

group A was 75.5 ± 22.5 min while it was 89.2 ± 20.6 min in group B (Table 1).

3.3. Postoperative data

The mean hospital stay in group A was 1.2 ± 0.7 days while it was 4.7 ± 1.8 days in group B. The mean levels of amylase were 62.0 ± 20.6 IU/l and 246.7 ± 121.4 IU/l in both groups, respectively. The mean level of lipase in group A was 53.5 ± 33.5 IU/l. Its level in group B was 247.2 ± 134.6 IU/l. According to Clavien- Dindo classification [9] of postoperative surgical complications, grade 1 complications occurred in 77 children, grade 2 occurred in 15 children while grade 3 developed in 4 cases in group A. In group B, grade 1 complications developed in 12 children, grade 2 occurred in 5 children and grade 3 complications occurred in 24 cases (Table 2).

Multi variant analysis was performed to correlate operative and postoperative variables to predictors of difficulty of laparoscopic splenectomy. Then, the assumed score was built up (Tables 3 and 4).

The Receiver Operating Characteristics (ROC) analysis was performed to examine the ability of the score to predict the prognosis of LS in children with benign hematological diseases. The area under the curve (AUC) was 0. 0780 (P < 0.001) indicating predictive ability to predict the outcome. The score carried the sensitivity of 91.8% % in predicting the outcome with cutoff value of 5 (Table 5 and Fig. 1).

The correlation between the outcome variables and the total score using Pearson correlation showed significant relation with operative time, hospital stay, pancreatic injury and postoperative complications (Table 6).

To validate this score, the study participates were divided into three groups according to the chosen cut-off value: no risk group (total score of <5 n = 46), moderate risk group (score of 5 till 8 n = 58) and high-risk group (score of 9–11 n = 33). (Table 7).

4. Discussion

LS has become the first choice among pediatric surgeons to manage children with benign hematological disease. It presents many advantages as it is more exploratory, safe procedure, lesser postoperative pain, shorter hospital stays, more cosmetic results with parents' satisfaction when compared to conventional open splenectomy [10,11].

Despite the advantages of LS, there is still a strong need to stratify children in categories to detect whom may have difficult operative course or have postoperative complications.

Some authors aimed at developing a difficulty score of LS to prepare patients with more investigations, plan B activation and competent surgeons to operate. However, difficulties and postoperative

Table 2
Univariate analysis of group A and group B in the model development dataset regarding postoperative data.

	Group A (n = 96)		Group B (n = 41)		P
Hospital stay (Median in days)	1		3		0.001*
Range	1–3		2–5		
Pancreatic injury	62.0 ± 20.6		246.7 ± 121.4		-
- Amylase Mean ± SD(ml)	53.5 ± 33.5		247.2 ± 134.6		0.001*
- Lipase Mean ± SD (ml)					0.001*
Dindo classification of surgical complications (No. of cases)					0.014*
Grade 1	77	80.2%	12	29.26%	
Grade 2	15	15.6%	5	12.19%	
Grade 3	4	4.16%	24	25%	

Table 3
Multiple variant analysis of predictors and outcomes.

	Operative Time			Postoperative Complications			Pancreatic Injury			Lipase			Hospital Stay		
	OR	95%CI	P	OR	95%CI	P	OR	95%CI	P	OR	95%CI	P	OR	95%CI	P
Hematological disease	Ref			ref			ref			ref			ref		
- ITP	10.29	1.23–85.84*	0.001*	1.07	0.27–4.22		0.55	0.13–2.32	0.002*	0.55	0.13–2.32		0.91	0.24–3.48	
- Spherocytosis	15.23	4.42–52.52*	0.001*	4.06	1.43–11.55*	0.001*	1.69	0.61–4.63	0.014*	1.49	0.54–4.14	0.014*	2.76	0.99–7.64	0.001*
- Thalassemia	7.17	2.16–23.78*		1.66	0.58–4.78		0.51	0.16–1.58		0.41	0.12–1.356		0.71	0.23–2.17	
- Sickle cell anemia	Ref			ref			ref			ref			ref		
Splenic pedicle control	0.178	0.07–0.47*	0.013*	0.33	0.09–1.13	0.015*	0.24	0.05–1.23	0.023*	0.14	0.02–1.23	0.001*	0.37	0.09–1.53	0.001*
- BSD	3.06	1.23–7.65*		2.25	2.09–13.20*		5.19	1.92–14.06		6.22	2.20–17.58		6.79	2.50–18.41*	
- Hem-o-lok	3.91	1.92–7.95*	0.001*	6.20	2.65–14.47	0.001*	4.05	1.66–9.89*	0.001*	5.58	2.10–14.81	0.021*	5.23	2.16–12.66*	0.015*
- Linear stapler	19.03	5.54–66.36*	0.023*	1.71	0.67–4.35	0.023*	0.68	0.28–1.67	0.015*	0.60	0.24–1.50	0.001*	1.04	0.42–2.59	0.325
EABL (median in ml)															
<150 ml vs > 150 ml															
Splenic long axis (median in cm)															
<12 cm vs > 12 cm															

Table 4
The assumed prognostic score of laparoscopic splenectomy in children with benign hematological diseases.

Predictors	Scoring
Pathology	
ITP	1
Spherocytosis	2
Thalassemia	3
Sickle cell anemia	4
Splenic long axis	
< 12 cm	1
>12 cm	2
Pedicle control	
BSD	1
Hem -o- loc	2
Endoscopic linear Stapler	3
Blood loss	
≤150 ml	1
>150 ml	2
Maximum total	11

BSD: bipolar sealing device.

Table 5
Agreement (sensitivity, specificity and accuracy) for total score with outcome.

ROC Curve	Cutoff	AUC	P	Sensitivity	Specificity
Score	5	0.780*	0.001	91.8%	52.9%

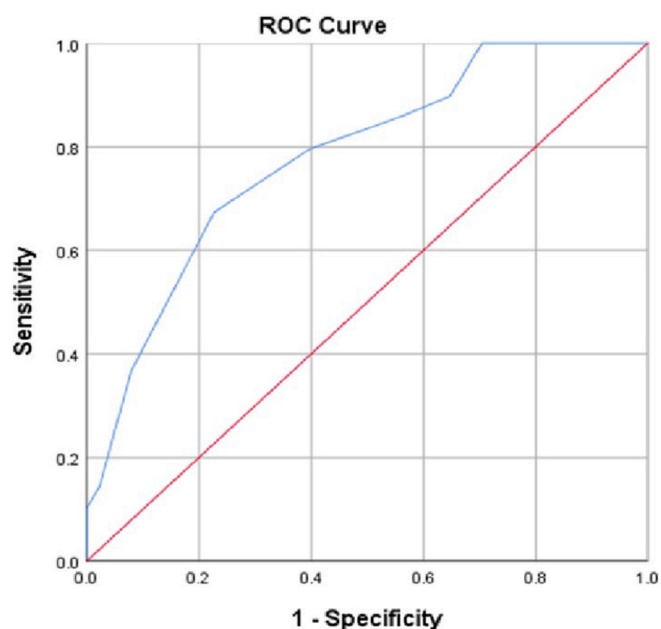


Fig. 1. ROC curve of specificity and sensitivity of assumed score.

Table 6
Correlation between total score and outcome variables, Pearson correlation.

Outcome variables	Total score	
	r/rho	p
Operative time in minutes	0.568	0.001*
Hospital stay in days	0.370	0.001*
Pancreatic injury		
- Amylase	0.298	0.001*
- Lipase	0.307	0.001*
Postoperative complications	0.724	0.001*

complications are still present even with expert surgeons [12].

Two main issues are involved when discussing LS in children. These issues are rate of conversion to conventional open splenectomy and learning curve of the procedure.

As regard to the conversion of LS to open splenectomy, it is considered by several authors to be a primary outcome or end point of any difficulty scoring system. They studied the effect of preoperative and operative factors that may predict increasing rate of conversion. These factors included the weight of spleen and to some extent the fragile nature of spleen. Other factors included bleeding tendency and disturbed coagulation profile, decrease platelets count and increased frequency of blood transfusion. This may lead to sever intraoperative bleeding and termination of the laparoscopic procedure. There is a proportional relation between the occurrence of intractable bleeding during LS and the rate of conversion [13,14].

The rate of conversion of LS to conventional surgery may reach up to 35% in some reports. This conversion is not considered a complication rather than a safe step to reduce the incidence of morbidity or even mortality. This decision may increase hospital stay, total costs and may be associated with patients' disappointment. The role of scoring system of LS difficulty is crucial to select the patient who is suitable to such procedure apart from occurrence of any post-operative complications [6].

Learning curve played an important role to master technique and reduce the personal factors that may lead to either operative difficulties or postoperative complications. Some authors assumed that a minimum of 20 cases was required to establish a safe LS [14].

Our study was designed to exclude cases that were converted to open splenectomy. This mainly was to build up a prognostic score of LS in children that may help to standardize technique in children and reduce to a great extent postoperative complication and hospital stay. The assumed prognostic scoring system aimed at incorporating preoperative factors as size of spleen and pathology together with method of pedicle control and estimated amount of blood loss.

There is significant relation between the nature of hematological disease and the outcome of LS. Children with SCA had the most difficult operative and prognostic courses. This was mainly explained by the natural pathology of the condition as it was associated with extensive peri-splenic adhesions due to healing of attacks of sequestrations. On the other hand, LS due to ITP had much better prognosis. Splenic size is usually small and no adhesions. Methods of controlling pedicle of spleen affect the prognosis. During current study authors depended on the mean length of splenic long axis as an index of splenic size. The longer this axis the more difficult the procedure. This was mainly attributed to decrease the laparoscopic space. Detecting the long axis of spleen was estimated by abdominal ultrasound. This helped to reduce unnecessary exposure of children to high doses of ionized radiation of CT.

Using BSD was associated with shorter operative time and lesser needs to more dissection along the course of splenic vessels and tail of pancreas. In contrast to the use of either Hem-O-Lok or endoscopic linear stabler which required skeletonization of adequate segment of pedicle. This was associated by increased of the mean EABL, longer operative time and increased manipulation on pancreas and pancreatic injury.

Cases with increased EABL were associated with longer hospital stay, more risk of pancreatic injury and higher incidence of complications.

This assumed score helped our team to stratify children into three groups according to postoperative prognosis. These groups are low, intermediate and high-risk group.

The conversion of LS to conventional open splenectomy was the main issue of Peng and his colleagues. They developed a scoring system that depended on three preoperative factors, weight of spleen, INR and esophagogastric varices. This mainly was to predict technical difficulties of the procedure as occurrence of sever bleeding. They excluded cases that had high score according to their study. Also, there was insignificant effect of the pathological conditions of spleen on the primary outcome. This score was designed to deal with certain conditions, adult

Table 7
Stratification of children according to prognostic score into three risk groups.

Variables	low risk		Moderate risk		High risk		p
	(n = 46)		(n = 58)		(n = 33)		
Etiology							
ITP	36	78.3%	0	0.0%	1	3.0%	
Thalassemia	8	17.4%	22	37.9%	13	39.4%	0.001*
Spherocytosis	1	2.2%	25	.1%	11	33.3%	
SCA	1	2.2%	11	19.0%	8	24.2%	
Pedicle control							
Bipolar sealing devices	24	52.2%	10	17.2%	13	39.4%	
Hem-o-lok	11	23.9%	30	51.7%	4	12.1%	0.001*
Stapler	11	23.9%	18	31.0%	16	48.5%	
Operative time(mean and SD)	61.3	±14.7	87.5	±22.1	91.6	±18.5	0.001*
Pancreatic injury	33	±12.5	54.6 ±	12.5	88.7	±13.2	0.014*
- Amylase (mean and SD	23.9	±5.9	76.3±	17.3	97.5	±15.3	0.001*
- lipase (mean and SD)							
Postoperative complications (%)	25	18.24%	55	40.14%	57	41.6%	0.023*
Hospital stay (mean ± SD)	1.4	±1	1.7	±1.1	2.3	±2	0.010*

patients, and certain ethnic groups of people. These considerations limit the validity of assumed score to be applied on children [15].

Luppi and his colleagues studied anatomical, clinical, and pathological factors that may affect the difficulty of LS. These factors were age, sex, splenic weight, and pathology. All these factors were preoperative and designed to predict difficult cases to be excluded from laparoscopic approach. These parameters were preoperatively investigated and determined. However, some factors as pedicle control maneuvers and EABL were not assessed. Also, this grading system was mainly applied in adult patients [6].

Some unique complications may occur during LS in children. Pancreatic injury is one of these complications. It is not related to any preoperative factors but mostly related to the way by which pedicle was controlled. Chand documented that pancreatic injury was the main complication that occurred in his series. The notable issue during his study was the use of endoscopic linear stapler to control the pedicle [16].

During the current study, it is observed that the incidence of pancreatic injury increases when endoscopic stapler used to control the pedicle. This may be explained by the need to dissect a considerable length of splenic pedicle to fit the stapler jaw. Due to the anatomical relation of the distal pancreas and the splenic hilum, the dissection is

carried out near the tail of pancreas and may cause injury.

With the application of Clavien-Dindo classification of postoperative complications during LS in children, the current study showed that the reported complications were associated with difficult cases where there was splenomegaly, prolonged operative time, increased amount of blood loss or use of endoscopic staplers.

Goncalves depended on Clavien-Dindo classification to describe the pattern of complications following LS in their cohort. They found that the rate of complications was increased when there were prolonged operative time, bleeding of more than 500 ml or conversion to open splenectomy [12].

The limitations of the current study are that it is retrospective single center experience.

However, according to available data this is the first study designed to develop a prognostic score of LS in children with benign hematological diseases (Table 8).

5. Conclusion

The assumed prognostic score of LS in children can stratify patients according to the prognosis of the procedure and predict whom children may be at risk of developing postoperative complications. Also, it is

Table 8
Different scoring systems in similar studies.

	Age group of patients (years)	Sample size (No. of patients)	Type of study	Pathological conditions	Aim of scoring system	Assessed variables
Current study	8 (4–15) years	137	Retrospective cohort	Benign hematological diseases	Prognostic	- etiology - splenic size - pedicle control - blood loss during LS
Luppi (6)	40 (3–88)years	439	retrospective study	- ITP - Other benign conditions - Malignant	Technical difficulty	- Age - Gender - Pathology - Splenic weight (g) - Difficulty grade
Goncalves (12)	38(18–88)years	153	Retrospective	- ITP - Benign lesions - Malignant	Validation of difficulty grading score	- Age - Gender - Pathology - Splenic weight (g) - Difficulty grading
Peng (15)	46(36–54.5) years	272	Randomized study	- Hypersplenism - Benign lesions - Malignant	Prediction of difficulty	- Splenic weight(g) - EGV - INR

LS: laparoscopic splenectomy.

EGV: Esophagogastric varices.

INR: international normalization ratio.

specific to age group and particular group of diseases of that age group.

Provenance and peer review

Not commissioned, externally peer reviewed.

Ethical approval

Research has obtained ethical approval by Ethical Board Review: Approval code 33872/6/20. Faculty of Medicine, Tanta University.

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Conflicts of interest

Authors stated that there is no conflicts of interest.

Author contribution

Mohammad Gh. Khirallah: conceptualization, methodology, operative procedures writing, editing and supervision – Ebrahim Ali Kabbash: investigation, formal analysis, reviewing and editing - Nagi Ibrahim El-Dessouki: methodology, operative procedures and edition.

Registration of Research studies

Name of the registry: clinicaltrials.gov.
ClinicalTrials.gov Identifier: NCT04763733.

Consent

A signed informed consent was obtained from the parents of children subjected to the procedure.

Guarantor

Mohammad Gharieb Khirallah, assistant professor and consultant of pediatric surgery, Tanta University Hospitals, Tanta University.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.102463>.

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