ICIS Splenectomy Registry

Registry Protocol

Version 1,0

Prospective, Multi-center International Registry

on behalf of the

Intercontinental Cooperative ITP Study Group (ICIS)

Patient Registration please use the Entry Sheet available at:

http://www.itpbasel.ch/Splenectomy-Registry.114.0.html

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Summary

The Splenectomy Registry is a retrospective and prospective international registry of the Intercontinental Cooperative ITP Study Group (ICIS, www.itpbasel.ch) collecting clinical data of children with immune thrombocytopenia (ITP) who are considered for splenectomy. Splenectomy is an accepted therapy for children and adults with ITP, however, particularly in children there are many unresolved questions regarding pre-, peri-, and postoperative aspects. The aim of the registry is to evaluate the long-term effects and safety aspects of splenectomy in children with primary or secondary ITP. Additionally, indication, timing and technique of splenectomy (open or laparoscopic splenectomy), and infectious diseases associated with splenectomy will be studied. The management of registered patients will not be affected by the registry, which is an observational registry. For this purpose, an entry sheet will be filled out by investigators, when a splenectomy is considered for a child with ITP. After the splenectomy, a further data sheet will be sent by the ICIS data office in Basel, Switzerland. After this sheet, a yearly follow-up sheet will be sent and filled out by the investigators. Retrospective data of children already splenectomized are also registered. As a long-term registry, the Splenectomy Registry is designed for a minimum duration of 10 years with the potential to further extend its duration. Clinical data of children will be collected, which will be anonymized using a patient registry number (unique patient number, UPN). The data transfer will be performed electronically.

Background

Splenectomy is a therapeutic tool of the management of both children and adults with chronic immune thrombocytopenic purpura (ITP). It is rarely performed in patients with acute ITP. The spleen is considered as the main organ of antiplatelet antibody production (1, 2, 3). Moreover the splenic reticuloendothelial system is the major site of clearance of antibody coated platelets.

Splenectomy is an accepted and effective treatment of children and adults with chronic ITP, with a lasting response rate of 60% to 88% (4, 5, 6, 7). Provan et al state in their international consensus report, that splenectomy in childhood ITP is an effective treatment for pediatric ITP, however, that it is rarely recommended in children because the risk of death from ITP in childhood is extremely low (<0.5%), and because complications, primarily sepsis, remain a concern (16). Currently, there are no reliable predictors of the effect of splenectomy. Law et

al reported a retrospective study of adults with ITP treated with intravenous immunoglobulins (IVIg) and subsequent splenectomy. Patients with good responses to IVIg were likely to have good responses to splenectomy, whereas patients with poor responses to IVIg were unlikely to benefit from splenectomy (8). The follow-up time of patients who responded well to splenectomy ranged from 12 months (13 of 19 patients) to 8 years. Splenectomy is often delayed in children due to risks associated with this invasive procedure. Overwhelming postsplenectomy infection caused by encapsulated organisms limits its safety and has been reported to have a mortality rate of 1.6% (9). The risk is greatest in patients younger than 5 years of age. There is a potential for spontaneous remission, which is another important reason to delay splenectomy (10).

There are many unresolved questions of the preoperative and operative management of splenectomy. The practice guidelines issued by hematologists on behalf of the American Society of Hematology identified inadequate data to make evidence-based recommendations on the appropriate indications and timing for splenectomy on when the harms of splenectomy might outweigh its potential benefits, and on appropriate preoperative management (11).The technique of splenectomy includes open and laparoscopic approaches, but, the optimal method is still debated (12, 13, 14, 15). There is a need to assess the long-term response rate of children after splenectomy and to identify predictors of splenectomy failure.

Aim of the study

The Splenectomy Registry will prospectively investigate children with ITP who are considered for splenectomy. Retrospective data of patients with ITP who have been splenectomized are also eligible. The following aspects will be evaluated:

- Long-term response rate of splenectomy
- Preoperative, operative, and postoperative management of splenectomy
  – Indication of splenectomy
  – Timing of splenectomy
  – Infectious diseases associated with splenectomy
  – Technique of splenectomy
- Safety of splenectomy

Inclusion criteria

Children (≤18 years of age) with primary and secondary ITP.

The retrospective part of the Splenectomy Registry is open to every child with primary and secondary ITP, independently of the duration of ITP. The prospective part is open to every child with primary and secondary ITP, for whom a splenectomy is planned.

Exclusion criteria

There are no exclusion criteria

Diagnosis of primary and secondary ITP

Primary ITP

Criteria of diagnosis of primary ITP are according to international guidelines (16)

1. Low platelet count, i.e. < $150x10^9$/L (although the more recent Vicenza conference (17) suggested < $100x10^9$/L)
2. History and complete blood count, blood smear and bone marrow aspirate (optional), are compatible with a diagnosis of ITP. A bone marrow aspirate is recommended before eventual corticosteroid treatment.
3. No secondary causes for ITP, such as systemic lupus erythematosus, HIV infection, and lymphoproliferative disorders.

Secondary ITP

According to international guidelines (16).

Study design

The Splenectomy Registry is a retrospective and prospective, multi-center international registry on behalf of the Intercontinental Cooperative ITP Study Group. Several questionnaires will be send out by the central data office (Basel, Switzerland) of the Intercontinental Cooperative ITP Study Group and completed by each participant. Questionnaires will be distributed by the central data office of the Intercontinental Cooperative ITP Study Group (ICIS) at the University Children's Hospital Basel, Switzerland. After announcement and publication of the Splenectomy Registry, an Entry Sheet must be completed by investigators wishing to register a patient. The UPN (unique patient number) will be given by the investigator. Please note that initials of patient are not allowed (data privacy protection). The study number wil be given by ICIS. All following questionnaires will be sent out by the ICIS central data office at the appropriate time: The "first sheet"(prefilled by ICIS with the study number) before splenectomy is planned, and the follow-up sheets every 12 months, beginning approximately 1 month after splenectomy (Table 1). Access of the central data office is possible using internet access (s. administration of the registry, page 3)

Table 1

Form	Form-Nr	Content/Date of issue
Entry sheet	**01**	Registration of the patient when splenectomy of a patient with ITP is ***planned***
1st sheet	**02**	Splenectomy **was performed** **to be filled out within 3 months**
Follow-up-sheet Nr. 1	**03**	1 year after splenectomy was performed
Follow-up-sheet Nr. 2	**04**	2 years after splenectomy was performed
Follow-up-sheet Nr. 3	**05**	3 years after splenectomy was performed
Follow-up-sheet Nr. 4 etc.	**06**	Follow-up sheets as reminders every year

The “Entry Sheet” and the “Follow-up Sheets” consist of one page. The 1st Sheet consists of 3 pages. The Intercontinental Cooperative ITP Study Group advertises the Registry regularly.

Data collection and evaluation

Data collection is performed through the Intercontinental Cooperative ITP Study Group by its central data office at the University Children's Hospital Basel, Switzerland. Each patient may be registered using online Entry Sheet, regular mail, fax, or e-mail, for address and phone/fax numbers see page 3. Patient information is handled anonymously. A study number is assigned to each patient. The evaluation of the data will be performed by the study coordinator. The results will be analyzed and discussed by the Intercontinental Cooperative ITP Study Group at regular scientific meetings.

The registry is designed for a long-term observation period of a minimum duration of 10 years. Interims analyses are planned with an interval of approximately 5 years.

Administration of the Registry

Patient registration can be performed using the online entry sheet or by sending a filled and downloaded entry sheet (http://www.itpbasel.ch/Splenectomy-Registry.114.0.html)

Publication

Publications of the study data may be undertaken according to the publication guidelines of the Intercontinental Cooperative ITP Study Group (www.itpbasel.ch).

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