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Original research

Laparoscopic splenectomy for medically refractory immune thrombocytopenia (ITP): A retrospective cohort study on longtime response predicting factors based on consensus criteria

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HIGHLIGHTS

- The study follows consensus definitions of ITP, enabling proper comparison with medical studies.
- Response to splenectomy was achieved in 87.5% of the patients.
- Loss of response occurred in 30.2% of the patients in median after 3 (range 2–42) months.
- Response to preoperative steroids and postoperative rise in platelets predict long term response.
- Laparoscopic splenectomy is an effective and safe treatment option in patients with ITP.

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ABSTRACT

Background: Laparoscopic splenectomy has been proposed to be the standard therapy for adult patients with medically refractory immune thrombocytopenia (ITP). However, due to inconsistent definitions of response, variable rates of long term response have been reported. Furthermore, new medical treatment options are currently challenging the role of splenectomy. The aims of this study were to (1) analyze long term response after splenectomy according to recently defined consensus criteria, (2) identify possible predictive response factors. **Methods**: A case series of 72 consecutive patients with ITP undergoing laparoscopic splenectomy was retrospectively studied using univariate and multivariate analysis as well as logrank tests. **Results**: Median follow-up was 32 (2–110) months. Mortality was 0% and morbidity was 8.2%. Response to splenectomy was achieved in of 63/72 patients (87.5%). Loss of response occurred in 19/63 (30.2%) in median after 3 (range 2–42) months. Preoperative platelet counts after boosting with steroids and immunoglobulins as well as the postoperative rise in platelet counts were statistically significant factors for response upon both univariate and multivariate analysis, whereas age, gender, body mass index, ASA classification, disease duration, accessory spleens, splenic weight, conversion to open surgery, or perioperative complications were not. Patients with a postoperative rise in platelet counts >150,000/μL had a significant better chance on stable long term response than those with a smaller increment ($P < 0.001$). **Conclusions**: Laparoscopic splenectomy is an effective and safe treatment option in order to obtain stable long term response in patients with ITP. Perioperative platelet counts are predictive factors of long term response.

1. Introduction

Primary immune thrombocytopenia (ITP), formally known as idiopathic thrombocytopenic purpura or Morbus Werlhof, is an acquired autoimmune disorder leading to enhanced thrombocyte degradation in the reticuloendothelial system. As recently emerged, a further pathogenic mechanism for ITP is an

Abbreviations: ITP, immune thrombocytopenia; CR, complete response; R, response; NR, non-response; IgG, immunoglobulin; ASA, American Society of Anesthesiologists; BMI, body mass index.

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immunologically mediated reduction of platelet production in the bone marrow [1]. ITP is defined by a reduced platelet count lower than 100,000/μL without any other detectable reason [2]. ITP patients predominantly develop skin and mucosal bleeding, but many patients remain asymptomatic for long time. Though a major concern, the total risk for fatal hemorrhagic complications is low with reported bleeding associated mortality rates of 0.3–10% [3]. The bleeding risk and the hemorrhagic lethality rate increase with the patient's age [4,5]. In patients with platelet counts lower than 30,000/μL, first line medical treatment consists in corticosteroids [6], possibly in combination with intravenous immune globulins. Splenectomy is proposed as second line therapy for ITP [6]. Approximately 80% of the patients respond to splenectomy, among which approximately 66% experience long term remission without further therapy [7–16]. Therefore, prediction of the hematological outcome after surgery is important when referring ITP patients for splenectomy. The laparoscopic approach is advantageous in terms of shorter hospital stay, less postoperative pain, and lower complication rates [17–19]; however, hematological outcomes are not different to conventional splenectomy [8,15,20,21]. Numerous clinical studies on splenectomy for ITP have been published, but results are hardly comparable since there is a lack of consensus on standardized definitions and outcome criteria. The present study follows the definitions and response criteria as stated by the Vicenza Consensus Conference 2007 [2]. In this conference the major goal for treatment of ITP was defined as to provide a safe platelet count rather than correcting the platelet count to normal levels [2]. Therefore earlier studies on laparoscopic splenectomy for ITP using older and individual definitions for remission might give delusive results. In the light of these differently defined criteria of response, the aims of this retrospective cohort study were to (1) analyze long term response after splenectomy according to consensus criteria, (2) identify possible predictive response factors.

2. Patients and methods

The study was approved by the ethics committee of Muenster University (AZ 2009-490-f-S). Between 2001 and 2009, 96 consecutive patients underwent laparoscopic splenectomy for various hematological and oncological disorders at Muenster University Hospital. Among these, 73 patients with medically refractory ITP were identified. Patient characteristics and postoperative courses were studied from patient charts and the clinical data base system retrospectively. 37 patients were males (50.7%) and 36 (49.3%) females with a mean age of 50.6 ± 19.7 years (range 16–83) and a body mass index (BMI) of 27.0 ± 4.5 kg/m^2 (range 16.6–36.3). Median time from the first diagnosis of ITP and surgery was 11.5 months (range 3 months–33 years). Indications for splenectomy included patients who no longer responded to medical therapy (73/73), those with platelet counts < 10,000/μL (26/73), and those with recurrent bleeding (58/73; patients frequently had more than one indication for surgery). Preoperative medication included steroids (100%, 73/73), immunoglobulins (52%, 38/73), anti-D (6.8%, 5/73), rituximab (2.7%, 2/73), cyclosporine A (1.3%, 1/73), and azathioprine (1.3%, 1/73). 15 patients were preoperatively classified according to the American Society of Anesthesiologists (ASA) class I (20.6%), 37 patients ASA II (50.7%), 20 patients ASA III (27.4%), and one patient ASA IV (1.3%). All patients were vaccinated against pneumoccus, menigococcus, and haemophilus influenzae perioperatively.

2.1. Surgical procedure

All patients received single shot antibiotic prophylaxis with cefuroxime 1.5 g i.v. at least 30 min before skin incision. Laparoscopic splenectomy was performed in a standardized three-trocar technique. After dissection of the colosplenic, gastrosplenic, and splenophrenical ligaments, the splenic pedicle was divided with a laparoscopic stapler in accordance to the hanging-spleen-maneuver [22]. Capsule tearing and spillage of splenic tissue was carefully avoided. The spleen was removed using an extraction bag in which the spleen was morcellated. The entire abdomen including the lesser sac and the splenic cavity were thoroughly examined for accessory spleens, which were removed if present. A drainage tube as an indicator for postoperative bleeding or pancreatic fistula was placed in left upper quadrant routinely. These tubes were removed when lipase in the secretion was negative.

2.2. Follow up

Most patients (60.3%, 44/73) had a regular follow up at the Department of Hematology and Oncology of Muenster University Hospital. From patients that were followed by their general practitioners (39.7%, 29/73), a written informed consent was obtained and the follow up data were inquired from the general practitioners according to a standardized questionnaire. Hallmarks for follow up were splenectomy-related mortality and morbidity, post-splenectomy infections, course of platelet counts, occurrence of bleeding, and the need for further medical therapy related to thrombocytopenia.

2.3. Response and relapse criteria

Response and loss of response were related only to the event of laparoscopic splenectomy and were defined according to recent consensus criteria [2]:

Complete response (CR) Defined as a normal platelet count of >100,000/μL at day 30 after splenectomy, and discontinuation of medication. Spontaneous bleeding must be absent.

Response (R) Defined as a rise in platelet counts > 30,000/μL and <100,000/μL at day 30 after splenectomy, and at least the doubling of the baseline platelet count in absence of spontaneous bleeding, and discontinuation of medication.

Non-response (NR) Defined as a missing rise in platelet counts > 30,000/μL or an initial rise but return to values < 30,000/μL within 30 days postoperatively. The need to continue or to restart medical therapy such as steroids or others to sustain on normal platelet counts is also considered as non-response. Spontaneous bleeding within 30 postoperative days is considered as non-response.

Loss of response (only patients that initially reached CR or R) Every thrombocytopenic event with platelet counts < 100,000/μL (from CR) or < 30,000/μL (from R) or less than 2-fold level of platelet count compared to baseline (from R) is classified as a loss of response. Occurrence of spontaneous bleeding or the need for medication is also considered as loss of response.

2.4. Potential predictive factors

In order to obtain factors which might influence the long term hematological outcome of laparoscopic splenectomy in patients with ITP, the following variables were implicated for analysis: Age, gender, BMI, ASA classification, duration of the disease (defined as time from first diagnosis until laparoscopic splenectomy), response to preoperative IgG and/or steroid boosting (reflected as platelet count on admission according to the fact that all patients received a preoperative boost with IgG and/or steroids), presence of accessory spleens, splenic weight, conversion to open surgery, perioperative complications, postoperative rise in platelet counts.