ABSTRACT

Objective: It is well known that splenectomy increases the risk of infections, mainly those caused by encapsulated bacteria. These complications are related to higher mortality and lower survival rates in asplenic individuals. The purpose of this study was to assess the mortality of rats submitted to total splenectomy. Methods: this is an experimental study. Thirty-four rats were divided into two groups: Group 1 (n = 14): control animals, submitted only to laparotomy; Group 2 (n = 20): animals submitted to splenectomy. Both groups were subdivided into two subgroups: Subgroup A, male rats, and Subgroup B, female rats. The animals were observed during a 90-day period to assess their mortality. Results: The mortality of animals in Group 2 was 80% for males and 30% for females. No deaths occurred among the animals of Group 1. The splenectomized males had significantly higher mortality rates than the splenectomized females (p = 0.034). Conclusions: According to results of this study, total splenectomy increases mortality among rats. Murine females demonstrated greater resistance to the asplenic state, and therefore presented lower mortality rates when compared to male rats.

Keywords: Splenectomy; Spleen/surgery; Sepsis; Mortality; Sex distribution; Rats, Wistar

INTRODUCTION

Splenectomy is a common surgical procedure conducted mainly in trauma management but is also performed to treat many hematologic, immune, metabolic and oncological diseases. The medical literature mentions other indications for splenectomy, for example, portal hypertension, parasitic infections and other specific splenic conditions, such as hemangiomas, cysts and abscesses(1-5).

Until recently, the absence of the spleen was not considered a risk factor for severe complications. However, death from postsplenectomy sepsis has been a known factor since the late 19th century. This procedure was considered beneficial and with no risks for the
patient. Other studies on the spleen were conducted, and it was observed that its removal was useless in most cases and that there were high mortality and morbidity rates following the procedure\(^6-7\).

Currently, there is no doubt that asplenic patients are more susceptible to severe infections with high mortality, including overwhelming sepsis, meningitis and pneumonia\(^8-9\). In 1929, O’Donnell was the first to describe a human death caused by postsplenectomy sepsis\(^10\). However, in 1891, Bardach had already observed the high level of mortality of sepsis following peritonitis in splenectomized dogs. In 1919, Morris and Bullock developed a similar project in rats and obtained the same result\(^11\). It was only in 1952, after King and Shumacker’s report of five deaths due to severe infection in children who had been splenectomized to treat spherocytosis, that the medical community began to acknowledge the importance of the spleen\(^12\).

A review done by Singer of 2,796 splenectomized patients showed an incidence of 4.2% of sepsis and a mortality rate of 2.5%\(^13\). The risk of severe sepsis is sixty-fold higher after splenectomy than it is in the general population. This situation is even worse in children, particularly those under two years of age, elderly and among immunocompromised patients\(^14\). The estimated incidence of overwhelming sepsis is 8% among these patients. According to Pimpl, approximately 6 to 9% of splenectomized patients die because of septic complications, while only 1 to 5% of those that have a spleen die from infection\(^1\).

Postsplenectomy sepsis is caused mainly by encapsulated bacteria, namely \(Pneumococcus\), \(Meningococcus\) and \(Haemophilus influenzae\)\(^8-9,15\). However, among immunocompromised patients, including the elderly, infections are caused mostly by Gram-negative bacteria, primarily \(Escherichia coli\), \(Klebsiella\) and \(Pseudomonas\)\(^16\).

Disseminated intravascular coagulation and purpura fulminans (Waterhouse-Friderichsen syndrome) may complicate the infections caused by \(Pneumococcus\) and other bacteria\(^8-9\). Viral, fungal, parasitic and herpetic infections, which are commonly self-limited and of low risk in the general population, can become very severe in splenectomized patients and even lead them to death\(^9\).

Another serious postsplenectomy complication is pulmonary thromboembolism. The incidence of this condition may reach 35%. This complication is apparently not due to thrombocytosis, although the number of platelets may increase considerably in asplenic patients\(^1,17-18\).

Hematological diseases such as myeloid hepatosplenomegaly, leukemias and lymphomas, and metabolic disorders such as dyslipidemias have higher rates of morbidity and mortality when total splenectomy is indicated. Conservative surgeries are suggested to avoid this situation. Total splenectomy, on the other hand, may be inevitable in certain situations such as trauma or even in elective conditions (e.g., hypersplenism, idiopathic thrombocytopenic purpura and serious forms of spherocytosis)\(^1,5,18\). The benefits brought by this procedure must be weighted against the risks of splenectomy.

The purpose of this study was to assess the influence of gender upon the postsplenectomy mortality in an animal model.

**METHODS**

This study complied with the recommendations of the International Guidelines of Animal Protection and was approved by the Ethics Committee of the Department of Surgery of the Medical School of the \(Universidade Federal de Minas Gerais\), Brazil\(^19,20\).

Thirty-four Wistar adult rats of both sexes were studied, their weight would vary from 150 to 290 g. The animals were allocated to appropriate cages, each one containing up to five rats. Water and normal rodent chow were offered freely. The animals were randomized to the following groups:

- **Group 1** \((n = 14)\) = Control Group
  - Subgroup 1A \((n = 7)\) = males
  - Subgroup 1B \((n = 7)\) = females

- **Group 2** \((n = 20)\) = Splenectomized Group
  - Subgroup 2A \((n = 10)\) = males
  - Subgroup 2B \((n = 10)\) = females

The surgical procedures were conducted under general anesthesia with ethyl ether. In Group 1 the surgical procedure was limited to a median laparotomy followed by laparorrhaphy. In Group 2, laparotomy was performed and the animals underwent total splenectomy. The surgical incision was closed with continuous 4-0 nylon suture being used the layered technique.

The animals were observed during a period of 90 days, and their mortality was evaluated. Each rat that would die underwent a necropsy so the cause of death could be determined.

The weight of the animals in different groups was assessed by the Kolmogorov-Smirnov (KS) normality test to verify the Gaussian distribution of data. The Bartlett test was also applied to analyze the variances. If the data presented a Gaussian distribution and the same variances, the t-Student test would be applied to the unpaired samples with the purpose of verifying the homogeneity of the groups. The Fisher’s exact test was applied to compare the mortality between the groups and sexes. Survival curves of the splenectomized animals...
were plotted using the Kaplan and Meier method and then compared by the log-rank test. P-values < 0.05 were considered significant (Figure 1).

RESULTS

The weights of all animals were within the normal distribution curve (p > 0.10) (KS distance 0.2293 for Subgroup 1A, KS 0.1970 for Subgroup 1B, KS 0.2805 for Subgroup 2A and a KS 0.1582 for Subgroup 2B). The variances were not unequal (by Bartlett’s test): Subgroup 1A x Subgroup 2A (p = 0.1489) and Subgroup 1B x Subgroup 2B (p = 0.2876). The mean weight of Subgroup 1A was 237.0 ± 8.4 g, Subgroup 1B: 158.3 ± 2.5 g, Subgroup 2A: 237.1 ± 10.9 g and Subgroup 2B: 161.0 ± 2.7 g. There was no difference between the weights of the male animals (p = 0.9947) and the females (p = 0.4869; t-Student test) showing that the groups were homogeneous and could be compared.

All Control Group animals survived the experiment. Eight of the splenectomized males (80%) died while only three splenectomized females (30%) died. The animals in Subgroup 2A died on the 5th, 7th, 8th, 25th, 26th, and 54th days, while Subgroup 2B animals died on the 6th, 13th and 27th days.

When compared to the Control Group, with spleen, there was a greater mortality among the male (p = 0.0007) and female (p = 0.06) splenectomized animals. It was observed that the splenectomized males presented a higher mortality rate when compared to the splenectomized females (p = 0.034; RR = 2.67; CI: 0.98 and 7.22).

The survival curves of the splenectomized animals (p = 0.025) were discrepant. Numerically, the estimated hazard ratio for mortality in the splenectomized male rats relative to the splenectomized females was 3.943 (CI: 1.194 – 14.06).

All animals had sudden deaths. There were no apparent physical or behavioral changes preceding the deaths. No macroscopic abdominal or thoracic changes were found during the necropsy. There were no signs of hemorrhage, purulent fluid or lesions of organs and structures next to the spleen. No signs of atelectasis, pneumonia or pleural effusion were found.

DISCUSSION

According to literature, atelectasis of the left lower lobe of the lung is the most common postsplenectomy complication. Postoperative hemorrhage, subphrenic abscesses, pancreatitis, pneumonia, surgical wound infections, sepsis, pulmonary embolism and portal thrombosis are other serious complications of asplenic patients that were not observed in this study\(^3,8,21\).

Although the absence of the spleen is compatible with an apparently normal life, it should be emphasized that the asplenic state increases the susceptibility to many diseases, mainly to those of septic and thromboembolic origin. These complications represent the most common cause of death among these patients. The absence of the spleen causes a depletion of serum levels of at least two important opsonins: tuftsin and properdin. This reduction is partially responsible for the higher susceptibility to acute infections caused by encapsulated bacteria\(^22\).

Overwhelming sepsis is a well known severe complication that affects patients that have undergone total splenectomy. This condition occurs suddenly

![Figure 1. Survival curve of splenectomized male and female rats plotted by the Kaplan and Meier method.](image-url)
in previously healthy individuals that are affected by a seemingly trivial infection, such as tonsillitis or erysipelas. In a few hours, the infection becomes systemic and may lead to death in a matter of hours or days despite proper treatment. Children under four years of age and immunocompromised individuals, like the elderly and chronic patients, are at a higher risk for this complication\(^{(12,25)}\).

According to the results found in this study, splenectomized animals present high mortality that is more frequent in the first postoperative month. The rats die without showing any sign of debility, lack of appetite or adynamia that could suggest a clinical state of infection.

**CONCLUSIONS**
In conclusion, total splenectomy is a cause of death in rats, males being more affected than females. This verification strengthens the indication that the spleen should be preserved whenever possible.

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**REFERENCES**