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Postoperative Complications After Splenectomy for Hematologic Malignancies

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Objective
The authors analyzed the frequency and character of postoperative complications after splenectomy in patients with hematologic malignancies, and correlated these findings with preoperative conditions that could have predicted their outcome.

Summary Background Data
Splenectomy is performed for hematologic malignancies for diagnostic and therapeutic indications. The role of splenectomy for lymphoproliferative and myeloproliferative malignancies is complex and sometimes controversial.

Methods
The medical records of 135 patients undergoing splenectomies for hematologic malignancies at Roswell Park Cancer Institute from January 1, 1984 to December 31, 1993 were reviewed retrospectively. These included Hodgkin's disease (HD), hairy cell leukemia (HCL), non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), and a miscellaneous group.

Results
The overall postoperative complication and mortality rates for all patients were 52% and 9%, respectively. The complication rate was 63% for patients whose spleens weighed greater than 2000 g, and 29% for patients whose spleens weighed less than 2000 g ($p = 0.001$). Seventy-three percent of the postoperative deaths were due to septic complications, only one of which was caused by an encapsulated organism. Complications occurred in less than 20% of patients with the diagnosis of HD and HCL; more than 50% of patients with NHL, CLL, and CML suffered postoperative complications.

Conclusions
Splenectomy performed in patients with hematologic malignancies is a potentially morbid procedure. Splenic size was the only preoperative factor found to be predictive of postoperative complications. The complication rate differed significantly between the different diagnostic subgroups.

Splenectomy has a diagnostic and therapeutic role in the treatment of hematologic malignancies. The role for staging laparotomy in Hodgkin's disease (HD) has become much more selective over the years as the population of patients who may benefit from the information gained has been better defined.[1] The role of splenectomy for lymphoproliferative and myeloproliferative malignancies is complex and sometimes controversial. Various rationales have been proposed for performing splenectomy in this group of patients, including improvement in hematologic parameters (either to reduce transfusion requirements or to improve tolerance for additional chemotherapy), staging, diagnosis, or relief of local symptoms resulting from massive splenic enlargement.

The potential clinical benefit must be weighed carefully against the potential for postoperative complications. Complications commonly reported after splenectomy include bleeding, pulmonary complications, subphrenic abscess, injury to adjacent organs, and sepsis.[2] It is to be expected that the complication rate in patients with hematologic malignancies may be higher than the general population because of their underlying medical condition.

The purpose of this study was to analyze the frequency and character of early and late postoperative complications after splenectomy in patients with hematologic malignancies and to correlate these findings with preoperative conditions that could have predicted their outcome.

PATIENTS AND METHODS

The medical records of 135 patients undergoing splenectomies for hematologic malignancies at Roswell Park Cancer Institute between January 1, 1984 and December 31, 1993 were reviewed retrospectively. The type of hematologic malignancy, length of hospitalization, operative blood loss, transfusion requirements, hematologic parameters, splenic size, postoperative complications, and survival from the time of splenectomy were analyzed. Any complication or death occurring within 30 days of splenectomy was considered an early complication. Any event occurring more than 30 days after splenectomy was considered a late complication.

The 135 patients were divided into six diagnostic groups to allow for analysis (Table 1). These included patients undergoing splenectomy for the following 1) HD, 2) hairy cell leukemia (HCL), 3) non-Hodgkin's lymphoma (NHL), 4) chronic lymphocytic leukemia (CLL), 5) chronic myelogenous leukemia (CML), and 6) miscellaneous hematologic malignancies. The latter group included 13 patients with acute myeloid leukemia (4 patients), myelofibrosis (2 patients), agnogenic myeloid metaplasia (1 patient), megakaryocytic leukemia (1 patient), myelodysplastic syndrome (1 patient), mycoses fungoides (1 patient), Waldenstrom's macroglobulinemia (1 patient), idiopathic thrombocytopenic purpura (1 patient), and aplastic anemia (1 patient).

Fifty-three individuals made up the group of patients with HD. Splenectomy was performed as a staging procedure alone in 45 patients and for both diagnostic and therapeutic reasons in 8 patients. Nine patients were clinical stage I (7A,2B), 34 were clinical stage II (29A,5B), 5 were clinical stage III (2A,3B), and 5 were clinical stage IV (2A,3B). Staging was based on the Ann Arbor classification.[3] Splenectomy was performed in stage IIIB and stage IV patients after chemotherapy failed, for diagnosis of a persistent mass or for symptoms of hypersplenism. Eight of the 53 patients (15%) received chemotherapy or steroids before undergoing splenectomy.

The group of patients with NHL was composed of 21 patients. Splenectomy was part of a staging procedure in three patients. Five patients had splenectomies for diagnoses of unexplained splenomegaly. Twelve patients had splenectomies performed for hypersplenism and increasing requirements for either erythrocyte or platelet transfusions. One additional patient underwent splenectomy before receiving a bone marrow transplant. Fourteen of the 21 patients (67%) received chemotherapy and/or steroids prior to splenectomy.

Splenectomies were performed in 19 patients with a diagnosis of CLL. Two patients in this group underwent splenectomies for symptomatic splenomegaly. One additional patient had a splenectomy for diagnostic purposes. The remaining 16 patients underwent therapeutic splenectomies for symptoms of hypersplenism. All 19 patients with CLL received chemotherapy before their splenectomies.

Eighteen individuals with CML underwent splenectomies. Three patients had splenectomies performed for symptomatic enlargement. Five patients were classified with hypersplenism. Six patients underwent splenectomies at the time of blast crisis to facilitate additional chemotherapy. Two patients underwent splenectomies for diagnosis, and the remaining two patients had splenectomies before bone marrow transplantation. Fifteen of the 18 patients (83%) received chemotherapy before splenectomy.

In the group of miscellaneous hematologic malignancies, splenectomy was performed for symptoms of hypersplenism in all but one patient. The latter patient with acute myeloid leukemia underwent splenectomy for

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Table 1. CHARACTERISTICS OF 135 PATIENTS WITH HEMATOLOGIC MALIGNANCIES

Diagnosis	Patients	Male/Female	Age Mean/ Range (yrs)	Mean Length of Hospitalization (days)	Mean Blood Loss—mL (range)	Mean Splenic Weight—g (range)	Mean Units of Transfusion
HD	53	33/20	30/12-68	17	587 (0-2826)	290 (120-1050)	<1
HCL	11	10/1	59/38-82	15	1225 (0-5250)	1749 (530-3850)	1.5
NHL	21	13/8	52/19-78	24	1191 (150-5000)	1705 (270-4000)	2
CLL	19	13/6	61/43-81	21	1062 (100-6000)	1862 (250-3830)	2
CML	18	8/10	53/31-74	22	875 (150-3000)	1754 (260-3125)	1
Misc	13	12/1	51/17-76	22	1623 (400-4000)	1540 (200-3500)	3

HD = Hodgkin's disease; HCL = hairy cell leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; Misc = Miscellaneous.

splenic pyogenic abscesses. A variety of chemotherapeutic and steroid regimens were administered to eight (62%) of these individuals before their splenectomies.

The operations were performed by senior staff surgeons and surgical oncology fellows. The approach was either through a left subcostal or midline incision. Drains were not used routinely. Epsilon-amino-caproic acid infusions were started preoperatively in patients with thrombocytopenia and continued for 12 to 24 hours postoperatively. The routine use of epsilon-amino-caproic acid was instituted at Roswell Park to reduce hemorrhage caused by fibrinolysis, which was found to be an occasional, unpredictable complication of splenectomy among patients with hematologic malignancies.[4] During the operative procedure, platelets were transfused to thrombocytopenic patients ($<50 \times 10^9/1$) after the splenic artery had been ligated. Blood was transfused when necessary, and prophylactic antibiotics were given routinely. In this retrospective review, it was impossible to document which patients received pneumococcal vaccine preoperatively. However, it has been the policy of the surgical oncology department that all patients undergoing elective splenectomy should receive pneumococcal and *Haemophillus influenzae* type B vaccine.

Statistical Analysis

Survival data were calculated by the Kaplan-Meier method.[5] Tests of significance with respect to survival distributions were based on the log rank test. Significance was defined as $p < 0.05$.

RESULTS

The overall complication and mortality rates for all patients was 52% and 9%, respectively. The complication and mortality rates varied significantly between the six diagnostic subgroups. Early and late postoperative complications are listed by subgroups in Tables 2 and 3, respectively. When analyzed by diagnostic group, those individuals with HCL had the lowest early postoperative complication rate (18%). All complication rates are listed in Table 4, according to diagnostic subgroup.

Pulmonary complications were the most common morbidity, occurring in 31 patients (23%) within 30 days of surgery and 12 patients (9%) as a late complication. Pulmonary complications included atelectasis, pneumonia, bronchitis, and pleural effusion. Pathology was limited most commonly to the left chest. Infectious complications were the second most common postoperative morbidity. Six patients (4%) had early septic complications and seven patients (5%) had later septic events. Septic complications included central venous line sepsis, meningitis, bacteremia, and urinary tract infection. Two of the three early postoperative deaths, and six of the eight later postoperative deaths involved septic complications (3 patients with HD, 2 patients with CLL, and 1 patient respectively with NHL, CML, and mycoses fungoides). The causative organisms involved in these sepsis-related mortalities included *Staphylococcus aureus, Escherichia coli, Haemophillus influenzae, Pseudomonas sp, Enterobacter sp,* and *Candida albicans.*

Pancreatic injury occurred in ten patients (7%), all as early complications. Pancreatic injury included pancreatic fistula and pancreatitis. All patients were managed conservatively with bowel rest and total parenteral nutrition until resolution of their hyperamylasemia or fistulae. Pancreatic injuries did not occur more often in patients with large spleens. Injury occurred in two patients with spleens weighing more than 2000 g and in five patients with spleens weighing less than 2000 g. Weights were not available in three patients with pancreatic injury.

Postoperative hemorrhage occurred in two patients (1%). One patient was followed with serial hemoglobins and did not require re-exploration. The other patient de-

Table 2. EARLY COMPLICATIONS AFTER SPLENECTOMY

Diagnosis	Death	Postoperative Bleed	Pulmonary Complication	Subphrenic Abscess	Pancreatic Injury	Wound Problem	Sepsis	Other	Total
HD	—	1	4	1	4	1	3	1	15
HCL	—	—	1	—	—	—	1	—	2
NHL	1	—	11	2	3	1	—	—	18
CLL	1	1	10	2	—	1	1	1	17
CML	1	—	5	—	1	3	1	2	13
Misc	—	—	—	1	2	1	—	—	4
Total	3	2	31	6	10	7	6	4	

HD = Hodgkin's disease; HCL = hairy cell leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; Misc = Miscellaneous.

veloped a postoperative pulmonary embolus and developed an intra-abdominal bleed secondary to systemic heparinization. This individual required re-exploration for control of hemorrhage. The preoperative platelet counts in these two patients were $51 \times 10^9/1$ and $432 \times 10^9/1$, respectively. The weight of the spleens were 2600 g and 2100 g, respectively.

Wound complications included incisional hernia, wound infection, wound hematoma, and abdominal wall dehiscence in eight patients (6%). These complications occurred in seven patients within 30 days of surgery and in one patient as a late complication.

Subphrenic abscess occurred in seven patients (5%), all but one as an early postoperative complication. Causative organisms included *Escherichia coli* and *Enterobacter sp.* Two of these patients had a concomitant pancreatic injury. Several patients had no organism identified.

Other complications included a postoperative gastrointestinal hemorrhage, prolonged ileus, myocardial infarction, pulmonary embolus, and small bowel obstruction in one patient each, respectively. All but one of these complications occurred in the early postoperative period. Thrombocytosis occurred in the patient who developed a pulmonary embolus, but not until after the embolus occurred (7-day postoperative platelet count = $150 \times 10^9/1$, 30-day platelet count = $1072 \times 10^9/1$).

Preoperative exposure to chemotherapy or steroids was a common occurrence in this patient population. All patients with CLL had received chemotherapy or steroids before their splenectomies. Eighty-three percent of patients with CML, 67% of patients with NHL, and 62% of patients classified with miscellaneous hematologic malignancies were exposed to perioperative chemotherapy or steroids. Fewer patients with HCL (45%) or HD (15%) received perioperative immunosuppressant agents.

The size of the spleen also correlated with the frequency of postoperative complications. There were 87 spleens removed that weighed less than 2000 g, with a frequency of postoperative complications of 29%. In patients whose spleens weighed greater than 2000 g (30 patients), postoperative complication rate was 63%. This difference was statistically significant ($p = 0.001$).

Table 3. LATE COMPLICATIONS AFTER SPLENECTOMY

Diagnosis	Death	Postoperative Bleed	Pulmonary Complication	Suphrenic Abscess	Pancreatic Injury	Wound Problem	Sepsis	Other	Total
HD	4	—	3	—	—	—	—	1	8
HCL	—	—	—	—	—	—	—	—	0
NHL	—	—	—	1	—	1	2	0	4
CLL	1	—	4	—	—	—	3	—	8
CML	2	—	2	—	—	—	—	—	4
Misc	1	—	3	—	—	—	2	—	6
Total	8	0	12	1	0	1	7	1	

HD = Hodgkin's disease; HCL = hairy cell leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; MISC = Miscellaneous.

Table 4. POSTOPERATIVE COMPLICATION RATES (EARLY AND LATE)

Diagnosis	No. of Patients	Early Complication Rate (%)	Late Complication Rate (%)
HD	53	19	13
HCL	11	18	0
NHL	21	52	19
CLL	19	72	26
CML	18	50	17
Misc	13	31	31

HD = Hodgkin's disease; HCL = hairy cell leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; Misc = Miscellaneous.

Operative blood loss did seem to correlate with the frequency of postoperative complications. Ninety-eight patients (73%) had an operative blood loss of less than 1000 mL, with a postoperative complication rate of 32%. Thirty-seven patients (27%) had an operative blood loss of greater than 1000 mL, with a postoperative complication rate of 49%. This difference in complication rate approached, but did not reach, statistical significance ($p = 0.07$).

There were three (2%) early postoperative deaths in this patient population. One patient with CLL underwent splenectomy for thrombocytopenia secondary to hypersplenism. He died 23 days after splenectomy from sepsis. The causative organisms were *Escherichia coli* and *Staphylococcus aureus*. A patient with CML in blast crisis underwent splenectomy before receiving additional chemotherapy. She died 12 days after splenectomy from progression of her disease. Her hematologic parameters improved after splenectomy and before her death. The third early postoperative mortality occurred in a patient with a large cell lymphoma who developed a subphrenic abscess and died 13 days after splenectomy. The causative organism was not identified.

Eight patients (6%) died in the late postoperative period with complications related to their splenectomy. Six of these individuals died as a result of septic complications (septic shock, 2 patients; pneumonia, 4 patients). One additional patient died secondary to gastrointestinal perforation and sepsis. The remaining patient died of progression of disease. Late deaths occurred 2 to 24 months after splenectomy.

The median survival after splenectomy varied considerably based on the diagnostic subgroup (Table 5). Patients with CML and CLL had a median survival of less than 1 year. The overall median survival in the 135 patients was 39 months.

DISCUSSION

Splenectomy performed in patients with hematologic malignancies is a potentially morbid procedure. The risks and benefits must be weighed carefully for each individual. The overall complication rate of 52% in our series is comparable to other reported series of 14% to 61%.[6–18] The mortality rate in our series of 9% also corresponds to prior studies with mortality rates of 5% to 13%.[4,6–8,11]

The indication for splenectomy varied based on the diagnostic subgroup, and the indications for splenectomy have evolved over the past decade for hematologic diseases. Currently, more splenectomies are performed for cytopenias and anemias and fewer are performed for splenomegaly and HD.[19] The majority of patients in our study with HD underwent splenectomies as part of a staging procedure. Currently, fewer staging laparotomies are being performed for HD. Reasons include improved noninvasive imaging studies, a better understanding of the poor prognostic factors, and a trend to treat earlier stage patients with chemotherapy.[1] At Roswell Park Cancer Institute, only patients with stage IA disease with poor prognostic factors (males, mixed cellularity histology, greater than 3 supradiaphragmatic sites), and stage IIA patients without bulky mediastinal disease are offered staging laparotomy. Splenectomy also has been implicated in the development of secondary cancers. Although current data are inconclusive, there may be an increased risk of the late development of acute leukemia in patients treated with splenectomy and chemotherapy for HD.[20–22] These patients also may have a slightly increased risk of secondary solid tumors.[23] It is not clear at this point whether the increase risk of leukemia and solid tumors is imposed by only the chemotherapy or increased by splenectomy as well.[24]

Patients with HCL responded favorably to splenectomy with an improvement in their hematologic parameters. Splenectomy has been reported to improve blood counts in 98% of patients with HCL, owing to removal of splenic sequestration and reduction of plasma volume.[25] Unfortunately, most patients develop progressive pancytopenia within 1 year of splenectomy secondary to progressive marrow disease. Current effective treatments of HCL include deoxycoformycin and 2-chlorodeoxyadenosine with complete response rates of 60% to 90%.[26,27]

Splenic involvement in the lymphoproliferative disorders such as CLL or NHL often is a part of extensive or late-stage disease. The indication for splenectomy in this group of patients is either for symptomatic splenomegaly or hypersplenism. Most of the patients in these subgroups in our series had advanced or rapidly progressive disease. Most were unable to tolerate full courses of chemotherapy or irradiation. The estimated 2-year survival

Table 5. ESTIMATED 2-YEAR AND 5-YEAR SURVIVAL

Diagnosis	Patients	Death within 30 Days of Surgery	2-Year Estimated Survival (%)	5-Year Estimated Survival (%)	Median Survival
HD	53	0	84	78	†
HCL	11	0	100	78	†
NHL	21	1	49	32	24
CLL	19	1	32	16	11
CML	18	1	22	16	7
Misc	13	0	37	9	15
All patients	135	3	59	43	39

HD = Hodgkin's disease; HCL = hairy cell leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; Misc = miscellaneous.
† Median survival not yet attained.

for these patients was 32% and 49% for CLL and NHL, respectively, and this correlates with previously reported series.[4,15]

Hypersplenism often is used as an indication for splenectomy in patients with lymphoproliferative disorders such as CLL or NHL. In reality, hypersplenism is a misnomer used in this context. These patients more commonly have a persistent pancytopenia for a combination of reasons, including marrow infiltration, marrow suppression due to previous treatment, increased plasma volume, and splenic sequestration. The contribution of the spleen to these patients' pancytopenia cannot be accurately determined preoperatively. Improvement in hematologic parameters was observed in the majority of these patients in our series. Hematologic correction of pancytopenia after splenectomy in patients with lymphoproliferative malignancies has been reported as frequently as 90%, despite bone marrow involvement.[15] This translates into lower transfusion requirements in a substantial proportion of these patients and perhaps a better quality of life. It would be unreasonable to expect an impact on survival in this group of patients in whom splenectomy was performed for palliative reasons.

Increased tolerance to chemotherapy also has been proposed as a benefit from splenectomy in patients with lymphoproliferative malignancies. No randomized prospective study to evaluate this has been performed to date. Several retrospective studies have shown a marginal improvement in tolerance for chemotherapy secondary to an improvement in these patients' hematologic parameters.[28,29]

Similar indications for splenectomy in patients with myeloproliferative malignancies have been proposed. There was discussion in the early 1970s that splenectomy may delay or prevent blastic metamorphosis in patients with CML, which always proves to be fatal. Two randomized trials were performed to study this concept. Patients with early-stage CML were randomized to splenectomy or no splenectomy.[30,31] After splenectomy, no survival benefit or reduced rate of blast metamorphosis was observed in either study.

It also has been proposed that there may be an enhanced effect on bone marrow engraftment in patients undergoing bone marrow transplantation after splenectomy. In a single retrospective study involving 18 patients undergoing bone marrow transplantation for chronic granulocytic leukemia, there were 12 long-term survivors. Engraftment appeared to be more rapid in the six long-term survivors who had prior splenectomies. However, there was an increased incidence of graft-*versus*-host disease and septic complications in the individuals who underwent splenectomy.[32]

The majority (73%) of early and late postoperative deaths in our series were due to septic complications, only one of which was caused by an encapsulated organism (*Haemophilus*). The only preoperative parameter found to be predictive of an increased complication rate was large splenic size. Patients with spleens larger than 2000 g had a statistically significant higher complication rate (63%) than those patients with smaller spleens (29%). Intraoperative blood loss greater than 1000 mL also correlated with a higher complication rate (49%), as opposed to a 39% complication rate for intraoperative blood loss less than 1000 mL. However, the difference did not reach statistical significance. Complication rates differed significantly based on the diagnostic subgroup. Less than 20% of patients with HD and HCL developed complications. However, more than 50% of patients with NHL, CLL, and CML developed complications, and the median survival in these groups ranged from 6 months to 2 years. In this latter group of patients, the increased morbidity may be the result of the underlying medical condition rather than the technical aspects of splenectomy. Thus, splenectomy performed for hematologic malignancies may be a potentially morbid procedure,

and the benefits must be balanced carefully against the risks.

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