

Causes of Death among Patients Surviving at Least One Year following Splenectomy

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BACKGROUND: To assess the mortality (mostly long-term sequelae) of patients undergoing splenectomy, we carried out a population-based study in Sweden.

METHODS: Using the unique personal identification number assigned to each Swedish resident, we linked centralized hospitalization records with nationwide mortality data. After initially assessing risks within the first 12 months after splenectomy, we excluded deaths during the first year and computed standardized mortality ratios (SMRs) for 1,297 patients splenectomized for external trauma and 991 surgically treated for nonmalignant conditions of adjacent organs who were alive at 12 months following surgery. The general Swedish population was used as the comparison.

RESULTS: Both men and women undergoing splenectomy for external trauma had a 1.6-fold (SMR = 1.6) significantly elevated mortality risk, due mainly to circulatory diseases (particularly thromboembolism), alcoholism, digestive disorders, and external causes. Men also had a 28-fold increased mortality from septicemia and an excess of liver cirrhosis (mostly alcohol-related). Patients of both genders splenectomized for nonmalignant conditions had small but significantly elevated mortality overall (SMR = 1.4 to 1.5) reflecting excess risks for malignancies, diseases of blood-forming organs, external causes, and circulatory, respiratory, and digestive disorders. In addition, men had increased mortality from thromboembolism and pneumonia while women experienced elevated risks from septicemia.

CONCLUSION: The excess mortality resulted from functional postsplenectomy defects (including

sepsis and thromboembolism), behaviors increasing risk of traumatic splenic injury (eg, alcoholism), damage to other organs from the external trauma (eg, traumatic injury to the central nervous system/spinal cord), or the same or recurrent nonmalignant conditions for which surgery was performed (eg, gastric and duodenal ulcers). *Am J Surg.* 1996;172:320-323.

Splenectomy may be necessary to reduce life-threatening blood loss or prevent iatrogenic injury during complicated surgery involving adjacent organs, but conservation of splenic tissue has been an important objective due to increasing recognition of the spleen's functional importance.¹ Overwhelming sepsis is an unusual though well-described complication that has been quantified in only nine population-based studies,²⁻¹⁰ while quantification of risks for chronic diseases has been limited to two of these investigations,^{4,10} one restricted to cancer outcomes only.¹⁰ We used the centralized Swedish hospitalization inpatient registry to assess mortality risks following splenectomy, mostly focusing on long-term sequelae.

METHODS

The study utilized a computerized linkage of the Swedish Inpatient Registry (or IPR, containing centralized hospitalization data reported annually), the Total Population Registry (yearly recording of all Swedish residents), and the nationwide Causes of Death Registry (a continuously updated listing of all deaths). From the IPR we identified all admission records of patients undergoing splenectomy (*Swedish Classification of Operations and Major Procedures*, codes 5610, 5611) during 1965 to 1983, reviewed concomitant diagnoses and surgical procedures, and assigned patients to groups by reason for splenectomy. We limited the study population to patients splenectomized for external trauma or for surgical treatment of nonmalignant conditions of adjacent organs and initially calculated mortality risks within the first 12 months after splenectomy for each group.

The major emphasis of the study was on risks subsequent to the first year after splenectomy to further understanding of long-term sequelae and to minimize selection bias (eg, to eliminate the effect of any condition that would have been the indication for splenectomy). To this end, we excluded deaths within the first year of splenectomy and identified 1,297 patients in the external trauma group and 991 patients (602 treated for peptic ulcer) in the surgical accompaniment group who were alive at 1 year following surgery.

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TABLE I

Characteristics of Patients Undergoing Splenectomy in Sweden by Reason for Splenectomy and Gender, 1965-1983

Characteristic	Splenectomy Due to External Trauma			Splenectomy Accompanying Surgery for Nonmalignant Conditions		
	Men	Women	Both	Men	Women	Both
Mortality follow-up*						
Number of patients	899	398	1,297	574	417	991
Mean age at entry, years	29	31	29	55	56	56
Mean calendar-year at entry	1977	1976	1977	1977	1978	1977
Mean number years of follow-up	12	12	12	10	10	10
Total number of person-years at risk	9,906	4,617	14,517	5,280	3,888	9,168
Mean age at death	56	63	58	70	72	71
Number of deaths during follow-up*	89	37	126	203	120	323

* Excluding deaths within the first year after splenectomy.

We then ascertained person-years beginning 12 months subsequent to the discharge date for splenectomy until death, emigration, or the end of the observation period (December 31, 1989), whichever came first. The expected mortality rates were calculated using Swedish national sex-, age-, calendar-year-, and cause-specific mortality rates in 5-year age and time intervals. Standardized mortality ratios (SMRs) were calculated as the ratios of observed to the expected number of deaths and presented with their 95% confidence intervals (CI).

RESULTS

Patients splenectomized for external trauma were substantially younger (18.8% were under age 15 and 60.9% under age 30 at surgery) than those undergoing splenectomy for nonmalignant disorders of adjacent organs (only 0.4% were under age 15 and 3.7% under age 30; Table I). Since there was little gender difference in the mean age at entry or length of follow-up in either cohort (Table I), data are shown for both genders combined.

During the first 12 months after surgery, patients splenectomized for external trauma had a 5.2-fold mortality increase (95% CI = 3.5 to 7.5, based on 30 deaths) compared with the general population, mostly owing to a remarkably elevated mortality from external injuries (SMR = 23.0, 18 deaths). Within a year of splenectomy accompanying nonmalignant disease of adjacent organs patients had 2.2-fold (95% CI = 1.5 to 3.0, 35 deaths) overall risk, primarily resulting from a notable excess of digestive disorders (SMR = 16.2, 10 deaths), in contrast. The remainder of this report focuses on longer-term mortality (from 12 months to 25 years following splenectomy).

The long-term sequelae among both male and female patients splenectomized for external trauma were characterized by much smaller although significant increases in all-cause mortality (SMR = 1.6) due to alcoholism, circulatory diseases (particularly thromboembolism), digestive disorders, and external causes, especially central nervous system or spinal cord trauma (Table II). Men also experienced a 28.0-fold increase of septicemia, based on 3 deaths all before 1980, and a 5.0-fold elevation of liver cirrhosis, primarily

alcohol-related. Total mortality among the external trauma cohort declined significantly with increasing age at splenectomy (SMRs = 2.9, 1.8, and 1.1 at age less than 30, 30 to 59, and 60 or more years, reflecting 24, 57, and 45 deaths, respectively). There were no significant trends in mortality according to the length of the interval after splenectomy, nor in calendar year (eg, the time period during which the splenectomy was performed; data not shown).

Risks for long-term sequelae among both genders splenectomized in accompaniment with nonmalignant conditions were similarly lower than short-term risks, though still significantly increased compared with the mortality in the general population (SMR = 1.4 for men, SMR = 1.5 for women), due to elevated risks for malignancy (mostly lung, stomach, and other digestive cancers), diseases of blood-forming organs, circulatory diseases (mainly cerebrovascular disease), emphysema, digestive disorders, and external causes (particularly central nervous system or spinal cord trauma and toxicity related to alcohol or drugs; Table III). In addition, men had increased mortality from thromboembolism, respiratory diseases, and gastric and duodenal ulcers, whereas women experienced elevated mortality from septicemia, liver cirrhosis (nonsignificant, and confined to patients with alcoholism), and mental and nervous system disorders. Total mortality in those splenectomized for nonmalignant disorders declined significantly with increasing age at operation, but remained elevated during each calendar period of follow-up, except for a decline in deaths from septicemia and diseases of blood-forming organs following splenectomy in 1980 or later (data not shown).

COMMENTS

Fulminant postsplenectomy sepsis, documented since the early 1950s among children² and since the 1970s among immunocompromised and healthy adults,⁵ has been extensively studied in the first year postoperation, during which risks have been generally highest among infants and patients with malignant disease,⁶ but usually low among those splenectomized for external trauma or benign disease. Although risks may remain elevated for many years after splenectomy, long-term sequelae have not been evaluated as

TABLE II

Mortality Risks among 1,297 Patients Undergoing Splenectomy in Sweden Subsequent to External Trauma, All Latency Periods Combined Excluding First 12 Months following Splenectomy, 1965-1989

Cause of Death	Observed Number	SMR	95% CI
All causes of death	126	1.6	1.3-1.9
All malignancies	17	0.9	0.5-1.4
All infectious and parasitic conditions	5	9.7	3.1-22.7
Septicemia	3	18.8	3.8-54.9
Tuberculosis	1	6.2	0.1-34.8
Mental disorders	5	4.1	1.3-9.6
Alcoholism	4	5.8	1.6-14.8
Diseases of circulatory system	50	1.3	1.0-1.7
Arteriosclerotic heart disease	27	1.1	0.7-1.6
Cerebrovascular disease	6	0.9	0.3-2.0
Venous and thromboembolic diseases	4	4.8	1.3-12.3
Respiratory diseases	3	0.7	0.1-1.9
Pneumonia	2	0.8	0.1-2.9
Digestive system diseases	12	4.4	2.3-7.7
Gastric and duodenal ulcers	2	4.1	0.5-14.7
Cirrhosis of liver	4	3.9	1.0-9.9
All external causes of death	28	3.0	2.0-4.3
Trauma to CNS/spinal cord	14	4.2	2.3-7.0
Toxic effects	3	2.1	0.4-6.2

SMR = standardized mortality ratio; 95% CI = 95% confidence interval; CNS = central nervous system.

TABLE III

Mortality Risks among 991 Patients Undergoing Splenectomy in Sweden Associated with Upper Abdominal or Lower Thoracic Surgical Procedures, All Latency Periods Combined Excluding the First 12 Months, 1965-1989

Cause of Death	Observed Number	SMR	95% CI
All causes of death	323	1.6	1.3-1.6
All malignancies	66	1.3	1.0-1.7
All infectious and parasitic conditions	4	2.9	0.8-7.4
Septicemia	2*	4.4	0.5-16.0
Diseases of blood-forming organs	3	7.2	1.4-21.0
Diseases of circulatory system	159	1.3	1.1-1.5
Arteriosclerotic heart disease	84	1.1	0.9-1.3
Cerebrovascular disease	37	1.7	1.2-2.3
Venous and thromboembolic diseases	8	3.0	1.3-5.8
Respiratory diseases	25	1.7	1.1-2.5
Pneumonia	15	1.7	1.0-2.8
Emphysema	6	5.3	1.9-11.5
Digestive system diseases	26	3.7	2.4-5.4
Gastric and duodenal ulcers	8	5.2	2.2-10.3
Cirrhosis of liver	4†	2.0	0.5-5.2
All external causes of death	23	2.5	1.6-3.7
Trauma to CNS/spinal cord	6	2.3	0.8-4.9
Toxic effects	5	4.9	1.6-11.4

* Cause of septicemia not specified.

† Three-fourths due to alcoholism.

SMR = standardized mortality ratio; 95% CI = 95% confidence interval; CNS = central nervous system.

intensively, particularly in population-based studies.²⁻¹⁰ Based on our data, the excess mortality due to sepsis (eg, the observed rate in the splenectomized Swedish patients minus the rate occurring in the general Swedish population) was 0.2 per 1,000 person-years in both cohorts.

Only two earlier population-based investigations evaluated other long-term sequelae. These were 740 male Ameri-

can servicemen splenectomized for external trauma during World War II and followed up through 1974 for mortality,⁴ and a nationwide study of Danish patients splenectomized during 1977 to 1989 for traumatic rupture ($n = 1,103$) or for other reasons ($n = 5,212$) and followed up for cancer incidence only.¹⁰ An increase in pneumonia characterizing the American servicemen was not observed among the Swedish patients, perhaps due to improvements in antibiotic therapy between the American (1946 to 1974) and Swedish (1965 to 1989) investigations. The excesses of cerebrovascular and thromboembolic disorders in our survey were consistent with the elevated ischemic heart disease among the American servicemen, both potentially linked with splenectomy-related thrombocytosis. A related postsplenectomy circulatory disorder is thrombosis of the mesenteric or portal veins, which may present with symptoms of a serious digestive disorder.¹¹ Another similarity was among American and Swedish men splenectomized for external trauma was an increase in liver cirrhosis, which was confined to those Swedish patients with a hospital discharge diagnosis of alcoholism. The increase in liver cirrhosis among the American servicemen may also have been alcohol-related or associated with hepatitis B or C infections transmitted as a result of transfusions to compensate for blood loss associated with splenic injury.

Despite the advantages of our population-based linked-registry study of splenectomized patients, a major limitation was lack of information on medications, other treatments, behavioral characteristics (eg, patients splenectomized for external trauma may have been more accident-prone) or other potential confounding exposures such as cigarette smoking and alcohol consumption. Some of the elevated mortality in our study population was associated with functional postsplenectomy defects, including sepsis and thromboembolism. Notable in this regard was the absence of increased mortality from sepsis among those splenectomized in 1980 or later, when prophylactic vaccination against

Streptococcus pneumoniae was introduced in Sweden. Prophylactic pneumococcal vaccine and judicious use of antibiotics¹² are already widely recommended, and small doses of aspirin have been suggested to prevent thrombosis and related circulatory disorders.¹¹ Excess mortality also resulted from fatal injury to other organ systems (particularly brain and spinal cord) in conjunction with external trauma se-

vere enough to rupture or damage the spleen. In addition, the elevated deaths from alcoholism among the external trauma cohort probably indicate a predisposition of alcoholics to traumatic injury. Similarly, an increase in deaths appeared to result from the same or recurrent nonmalignant conditions (eg, gastric and duodenal ulcers) necessitating splenectomy in conjunction with surgical procedures involving adjacent organs. Historical comparisons of long-term sequelae subsequent to spleen-sparing procedures versus total splenectomy will require the passage of time. However, epidemiologic, laboratory, and medical record review studies of incident cases of sepsis and circulatory diseases following splenectomy or other patient subsets may be useful to clarify the host and environmental determinants of long-term sequelae, the mechanisms involved, and potential preventive measures for late complications after splenectomy.

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