Splenectomy Does Not Increase COVID-19 Risk or Mortality in Abdominal Cancer Surgery: A Retrospective Cohort Analysis

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What is already known on this topic?

- *Splenectomy is known to increase susceptibility to bacterial infections, but its effect on viral infections such as COVID-19 remains unclear.*

What does this study add to this topic?

- *This study shows that splenectomy in abdominal cancer surgery is not associated with increased risk of postoperative COVID-19 infection or mortality.*

Abstract

Objective: Splenectomy is frequently performed in abdominal malignancy surgeries due to direct tumor invasion, vascular injury, or for technical reasons. Although its association with bacterial infections is well documented, the effect of splenectomy on the risk and prognosis of viral infections, particularly COVID-19, remains unclear. To evaluate the incidence of postoperative COVID-19 infection and its prognostic impact in cancer patients undergoing abdominal surgery with and without splenectomy.

Methods: This retrospective, single-center study analyzed 337 patients who underwent abdominal surgery for malignancy between March 2020 and March 2022. Forty-four patients underwent splenectomy as part of their oncologic procedure. COVID-19 status, demographic characteristics, comorbidity burden (Charlson Comorbidity Index), and survival outcomes were compared between patients who underwent splenectomy and those who did not. Logistic regression and Kaplan–Meier survival analyses were performed.

Results: Postoperative COVID-19 infection occurred in 18.4% of all cancer patients and in 17.7% of those who underwent splenectomy. Splenectomy was not associated with a statistically significant increase in COVID-19 risk (odds ratio (OR): 1.58; 95% CI: 0.75-3.33; $P = .22$). This finding remained consistent after adjustment for comorbidities (OR: 1.50; 95% CI: 0.70-3.19; $P = .29$). Similarly, COVID-19 infection was not a significant predictor of mortality in the splenectomy group (adjusted OR: 1.02; 95% CI: 0.22-4.59; $P = .97$). Kaplan–Meier survival analysis revealed comparable overall survival between patients with and without splenectomy, with no statistically significant difference observed (log-rank test, $P = .54$).

Conclusion: Splenectomy in patients with abdominal malignancies was not found to be a risk factor for acquiring COVID-19 or for poor survival outcomes following infection. While this study suggests no detrimental effect of splenectomy on the clinical course of COVID-19 in patients with cancer, more comprehensive prospective investigations are necessary to support this conclusion.

Keywords: Abdominal malignancy, cancer surgery, COVID-19, immunocompromised, postoperative infection, prognosis, splenectomy

Introduction

A series of unexplained pneumonia cases surfaced in Wuhan, Hubei Province, China, in December 2019. These cases were subsequently linked to a novel coronavirus, later designated as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19. The widespread dissemination of COVID-19 by mid-2022 had accounted for more than 510 million confirmed cases and over 6 million global deaths.[1,2]

Individuals with cancer are especially susceptible to adverse outcomes from COVID-19, mainly due to their compromised immune systems, stemming from both malignancy and oncologic therapies. Upon contracting SARS-CoV-2, these patients commonly present with general symptoms including elevated body temperature, exhaustion, and a persistent dry cough.[3] Numerous studies

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have consistently shown that cancer patients experience higher morbidity and mortality rates when infected with COVID-19.[4]

The spleen serves a pivotal immunological function by filtering pathogens from the bloodstream and facilitating immune responses, particularly against encapsulated bacteria.[5] Playing a role in both arms of the immune system, the spleen facilitates the synthesis of IgM and supports the activation of the complement system. Splenectomy has been historically associated with a heightened risk of life-threatening infections, particularly from encapsulated bacteria such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*.[6,7]

While the risk of bacterial infections following splenectomy is well-documented, data on the susceptibility to and prognosis of viral infections, particularly SARS-CoV-2, remain limited. To date, the potential influence of splenectomy on the COVID-19 disease course among patients receiving surgery for abdominal malignancies has not been clearly defined. Given the immunological deficits following splenectomy and the inherent vulnerability of oncology patients, it is conceivable that this surgical intervention may modulate COVID-19 risk and prognosis in this group.

This study aims to evaluate the incidence of postoperative COVID-19 infection and its prognostic impact in patients who underwent splenectomy as part of surgical treatment for abdominal cancers and to compare them with matched cancer patients who did not undergo splenectomy during the same period.

Methods

Study Design and Patient Selection

Patients who underwent surgery for abdominal cancers at the center between March 2020 and March 2022 were retrospectively reviewed as part of this single-center study. The study population was identified through hospital records, and only patients who underwent surgery for histologically confirmed malignancies were included in the study. Patients who underwent splenectomy as part of their oncologic surgical procedure during the study period formed the splenectomy group, while those who underwent abdominal cancer surgery without splenectomy served as the control group.

Exclusion criteria were: (1) surgery for benign indications, (2) postoperative mortality within 30 days, and (3) incomplete or inaccessible clinical data. All patients included in the study provided written informed consent for the use of their medical and surgical data for research purposes. The study protocol was approved by the Ethics Committee of the Ankara University Faculty of Medicine and the Cebeci Hospital (Date: May 12, 2022 / No: E-22300087-622.03-507458) and was conducted by the principles outlined in the Declaration of Helsinki.

Data Collection and Definitions

Patient demographics (age, sex), surgical data, pathological diagnoses, COVID-19 test results, and clinical outcomes were extracted from electronic medical records. COVID-19 status was determined based on postoperative polymerase chain reaction testing. Pathological data included tumor histological type and staging. Tumor-node-metastasis (TNM) staging was conducted according to the American Joint Committee on Cancer eighth edition guidelines, with pancreatic cancers staged according to pancreas-specific criteria.

The Charlson Comorbidity Index (CCI) was used to assess comorbidity burden. Patients were categorized into 3 groups based on CCI score: low (CCI = 0), moderate (CCI = 1-2), and severe (CCI > 2). Overall survival (OS) was defined as the time from surgery to either death or the end of the study period (March 2022), whichever occurred first. Survival analyses were conducted stratified by COVID-19 status and splenectomy status.

Statistical Analysis

Descriptive analyses were applied to outline the baseline characteristics of the study population. Means and standard deviations were calculated for continuous variables, while categorical data were summarized as frequencies and proportions. Statistical differences between groups were assessed using chi-square or Fisher's exact tests for categorical variables, and the normality of continuous variables was first evaluated using the Shapiro–Wilk test. For normally distributed variables, the independent samples *t*-test was applied, whereas non-normally distributed variables were compared using the Mann–Whitney *U*-test.

Logistic regression analysis was used to assess the association between splenectomy and the risk of postoperative COVID-19 infection. Multivariable models were constructed by adjusting for potential confounders, including the CCI score. Odds ratios (ORs) with 95% CIs were calculated.

Overall survival was analyzed using the Kaplan–Meier method, and survival curves were compared using the log-rank test. All statistical tests were 2-tailed, and a P value < .05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Between March 2020 and March 2022, a total of 497 patients underwent abdominal surgery at the clinic. Of these, 134 were excluded because the indication for surgery was non-cancerous (e.g., benign disease, re-operation, laparotomy), and 26 patients were excluded due to death within 30 days postoperatively (Figure 1). Ultimately, 337 patients who underwent surgery with a diagnosis of malignancy were included in the final analysis. Among these, 162 (48.1%) were female and 175 (51.9%) were male. The mean age of the cohort was 59.3 ± 13.4 years.

A total of 62 patients (18.4%) were diagnosed with COVID-19 in the postoperative period. The demographic and clinical characteristics of COVID-19-positive patients are presented in Table 1. COVID-19 infection was found to be significantly more common in female patients (P = .02), and the mortality rate was substantially higher in COVID-19-positive patients compared to those without COVID-19 (P = .04). Furthermore, the CCI score was significantly higher among COVID-19-positive patients (P = .04), with a notable difference in the distribution of moderate and severe comorbidities compared to the control group.

A total of 44 patients (13.1%) underwent splenectomy during cancer surgery, while 4 additional patients had a prior history of splenectomy. In the clinic, splenectomy was performed in conjunction with oncologic surgery in 40 patients. The main indications included direct tumor invasion, iatrogenic injury to the spleen or its vessels, lymph node dissection requirements, and technical considerations. Among patients who underwent splenectomy during the pandemic, 11 (17.7%) were diagnosed with COVID-19 postoperatively. The most common cancer types requiring splenectomy were gastric cancer (n = 19, 30.6%), colorectal cancer (n = 18, 29.0%), and pancreatic cancer (n = 8, 12.9%).

Among COVID-19-positive patients, the descriptive characteristics stratified by splenectomy status are shown in Table 2. There were no significant differences between splenectomized and non-splenectomized patients in terms of age, gender distribution, or CCI score. Mortality occurred in 3 of 11 splenectomy patients (27.3%), all of whom were attributed to COVID-19-related complications.

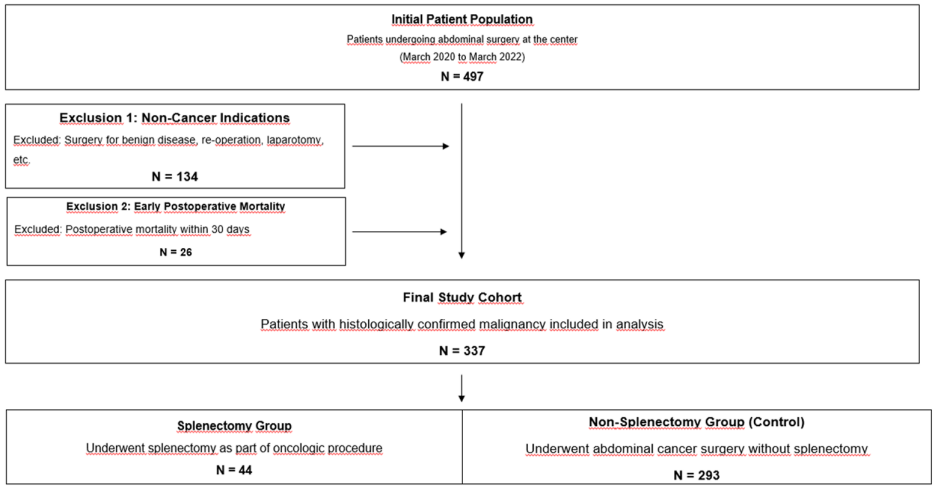

Figure 1. STROBE-compliant flow diagram of patient inclusion and exclusion.

Table 1. COVID-19-Related Characteristics

Characteristic	COVID-19 Positive (n = 106)	COVID-19 Negative (n = 257)	Total (n = 363)
Female (%)	51.9	45.5	47.4
Mortality (%)	23.6	23.0	23.1
Mean CCI Score	1.06	1.26	1.20

Table 2. Mortality in COVID-19-Positive Patients by Splenectomy Status

Outcome	No Splenectomy (n = 92)	Splenectomy (n = 11)	*P**
Survived	70	8	–
Died	22	3	–
Statistical comparison	–	–	**.23**

**P* reflects the original analysis reported in the manuscript.

However, the difference in mortality between the 2 groups was not statistically significant ($P = .23$).

The overall comparison between splenectomy and non-splenectomy patients in the study population is detailed in Table 3. Patients who underwent splenectomy were significantly younger than those who did not (mean age 54.7 vs. 59.8 years, $P = .015$). There were no statistically significant differences in gender distribution, CCI score, or mortality rates.

Table 3. Patient Characteristics by Splenectomy Status

Characteristic	Splenectomy (n = 44)	No Splenectomy (n = 293)	*P*
Mean age (years)	54.68	59.83	.015
Female (%)	52.1% (23/44)	46.7% (137/293)	.602
Mean CCI score	1.08	1.22	–
Mortality rate (%)	22.9% (10/44)	23.2% (68/293)	1.000

Multivariate logistic regression analysis demonstrated no significant association between splenectomy and the risk of postoperative COVID-19 infection (OR: 1.58; 95% CI: 0.75-3.33; $P = .22$). After adjustment for CCI score, the result remained non-significant (OR: 1.50; 95% CI: 0.70-3.19; $P = .29$). The CCI score was found to be an independent predictor of COVID-19 infection ($P = .021$), but splenectomy was not ($P = .88$).

Kaplan–Meier survival analysis revealed no significant difference in OS between the splenectomy and non-splenectomy groups (log-rank test, $P = .54$) (Table 4). Similarly, postoperative COVID-19 infection was not identified as a significant risk factor for mortality when comparing splenectomy and non-splenectomy groups (OR: 1.09; 95% CI: 0.25-4.76; $P = .90$). This remained consistent after adjustment for CCI score (OR: 1.02; 95% CI: 0.22-4.59; $P = .97$). No significant survival difference was observed in the Kaplan–Meier test between groups based on COVID-19 infection status ($P = .28$).

Discussion

The prolonged course of the COVID-19 pandemic has brought to light the heightened vulnerability of immunocompromised

Table 4. Kaplan–Meier and Mortality Risk Analysis

Comparison	Statistical Method	Result
Overall survival: splenectomy vs. no splenectomy	Log-rank test	$P = .54$
Mortality risk (COVID+): splenectomy vs. no splenectomy	Logistic regression (unadjusted)	OR = 1.09 (95% CI: 0.25-4.76), $P = .90$
Mortality risk (COVID+), adjusted for CCI	Logistic regression (CCI-adjusted)	OR = 1.02 (95% CI: 0.22-4.59), $P = .97$
Overall survival: COVID+ vs. COVID–	Log-rank test	$P = .28$

individuals. Those who have undergone splenectomy are among these at-risk populations due to the spleen's essential role in immunological defense mechanisms. Housing numerous lymphoid and phagocytic cells, the spleen is instrumental in mounting effective responses to encapsulated bacterial pathogens and select viral infections.[9,10]

Emerging evidence has shown that SARS-CoV-2 infection can directly affect splenic tissue, leading to atrophy of lymphoid follicles and a reduction in T and B lymphocyte populations.[11,12] Autopsy findings from patients who died due to COVID-19 have confirmed splenic atrophy, lymphoid depletion, and necrosis, suggesting direct or indirect viral effects on this immunologically active organ.[13] These findings raise concerns about the susceptibility and disease progression of COVID-19 in patients who have undergone splenectomy.

While the increased risk of bacterial infections post-splenectomy is well-documented,[6] the data regarding viral susceptibility, particularly to SARS-CoV-2, are limited. The study sought to address this gap by evaluating the incidence and outcomes of COVID-19 in splenectomized vs. non-splenectomized cancer patients who underwent abdominal surgery.

In the cohort, 18.4% of all cancer patients and 17.7% of splenectomized patients developed COVID-19 in the postoperative period. Splenectomy was not associated with a statistically significant increase in COVID-19 infection risk (OR: 1.58; 95% CI: 0.75-3.33; $P = .22$), and this finding remained consistent after adjusting for comorbidities (OR: 1.50; 95% CI: 0.70-3.19; $P = .29$). Similarly, COVID-19 infection did not significantly impact survival outcomes in splenectomized patients (adjusted OR: 1.02; 95% CI: 0.22-4.59; $P = .97$). Kaplan–Meier analysis revealed no significant difference in OS between the splenectomy and non-splenectomy groups (log-rank $P = .54$).

These results support the notion that splenectomy is not an independent risk factor for COVID-19 infection or mortality in cancer patients, consistent with recent findings showing comparable outcomes in vaccinated splenectomized patients.[14,15] Nevertheless, appropriate long-term preventive strategies remain essential. Guidelines recommend lifelong infection prophylaxis and vaccination, including against encapsulated bacteria and SARS-CoV-2, for patients with functional or anatomic asplenia.[16,17]

One of the key strengths of this study is its focus on a clinically relevant yet underexplored area, using real-world data from cancer patients during the height of the pandemic. The use of standardized comorbidity assessment (CCI), logistic regression, and survival analysis provides a comprehensive evaluation of risk and prognosis.

While the study contributes to the current understanding of COVID-19 in patients with splenectomy for cancer, it has notable limitations. Being retrospective and conducted at a single center, it may be subject to bias. One of the primary limitations of this study is the modest cohort size, particularly within the splenectomy group, which may limit the strength and generalizability of the findings. The absence of essential data, such as vaccination records, information on SARS-CoV-2 variants, and antibody response, also restricts the depth of analysis. Moreover, the heterogeneity of abdominal malignancies included could have influenced the variability in patient outcomes.

To conclude, the analysis shows no evidence that splenectomy increases vulnerability to COVID-19 or negatively impacts postoperative prognosis in abdominal cancer patients. These preliminary results may guide clinical decision-making, but should be substantiated by further prospective research involving larger cohorts.

One of the main strengths of this study is its focus on a clinically relevant but underexplored area—the potential impact of splenectomy on postoperative COVID-19 outcomes in cancer patients. To the best of knowledge, this is one of the few studies to investigate the incidence and prognosis of COVID-19 infection specifically in splenectomized patients undergoing abdominal cancer surgery. The study employed a standardized comorbidity assessment using the CCI and incorporated multivariable analysis to control for confounding factors. Additionally, the inclusion of a real-world cancer patient population during the height of the COVID-19 pandemic increases the clinical applicability of the findings. The use of survival analysis, specifically the Kaplan–Meier method, further strengthens the validity of the outcome assessment.

Several limitations to this study must be considered when evaluating its findings. Primarily, the retrospective nature of the analysis may have introduced selection and information bias due to reliance on pre-existing medical documentation. Second, the study was conducted at a single center with a relatively small sample size, particularly in the splenectomy group, which limits the generalizability of the findings and reduces statistical power. Third, although efforts were made to adjust for comorbidities using the CCI, other potential confounders such as vaccination status, viral load, and perioperative treatment regimens were not included in the analysis. Lastly, the heterogeneous nature of abdominal malignancies and surgical procedures makes it difficult to conclude specific cancer types or treatment pathways.

The present study explored the frequency and clinical impact of postoperative COVID-19 among patients with abdominal malignancies, particularly focusing on individuals who underwent splenectomy. Findings suggest that splenectomy is not associated with an increased risk of infection or decreased survival after surgery. In this cohort, splenectomy was not identified as an independent risk factor for either SARS-CoV-2 infection or poor prognosis.

Given the limited sample size and single-center, retrospective design, these findings should be interpreted with caution. Further large-scale, multicenter, and prospective studies are warranted to validate these observations and to better understand the immunological impact of splenectomy on viral infections, such as COVID-19, in oncology patients.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. It has been approved by the Ankara University Faculty of Medicine and the Cebeci Hospital (Date: May 12, 2022 / No: E-22300087-622.03-507458)

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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