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**ABSTRACT:**

**INTRODUCTION:** The perioperative mortality is significantly higher in patients with cirrhosis undergoing certain surgical procedures. In this study, we examined the inpatient perioperative mortality and morbidities in cirrhotic people who underwent laparoscopic appendectomy.

**METHODS:** We performed a retrospective analysis using the National Inpatient Sample database for 2010. Inclusion criteria were all race and sex who are 18 years or older. Those who have laparoscopic appendectomy and have a history of liver cirrhosis were assigned to case group. An equal random number of appendectomy-related admissions and those who have no history of liver cirrhosis were selected and placed in the control group. A binary logistic regression statistical test was used to examine the odds ratio for the mortality difference and postoperative complication including pneumonia, urinary tract infection (UTI), surgical site infection, postoperative bleeding. IBM SPSS statistics was used to execute the analysis. A confidence interval of 95% and *P* value less than .05 were determined to define the statistical significance.

**RESULT:** A total of 754 appendectomy-related admissions were identified—376 appendectomy-related admissions and history of cirrhosis and 378 admissions with appendectomy and no history of cirrhosis. Control group was not found to be statistically different from the case group when it comes to age, race, and sex. Of 754, 520 were white (73.5%), 334 (44.3%) were men. The mean age was 43.75 years for the case group and 46.68 years for the control group. Comparing cirrhotic with noncirrhotic group, the mean length of stay was 1.1 vs 1.52 days, inpatient mortality was 2 (0.5%) vs 1 (0.3%) ($P = .56$), pneumonia 8 (2.1%) vs 3 (0.8%) ($P = .142$), surgical site infection 3 (0.8%) vs 2 (0.5%) ($P = .652$), UTI 18 (4.8%) vs 12 (3.2%) ($P = .26$), and postoperative bleeding 3 (0.8%) vs 2 (0.5%) ($P = .65$).

**CONCLUSIONS:** Appendectomy-related morbidity and mortality in cirrhotic patients are not different from noncirrhotic patients.

**KEYWORDS:** Laparoscopy appendectomy, mortality, liver cirrhosis

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## Introduction

Liver cirrhosis represents a consequence of progressive hepatic fibrosis from recurrent injury characterized by disruption of the hepatic architecture and the formation of irreversible regenerative nodules commonly identified on imaging. The most common causes in the United States are hepatitis C virus (HCV) cirrhosis, alcoholic cirrhosis, and nonalcoholic steatohepatitis (NASH) cirrhosis accounting for 53.5%. With the current trajectory of increasing obesity, NASH-related cirrhosis is projected to be the most prevalent cause in future years.[1] Cirrhosis is a major cause for hospital admissions, readmissions, and financial expense and mortality. A study conducted in 2012 demonstrated that cirrhosis and its complications lead to more than 150 000 hospitalizations costing nearly US $4 billion each year.[2] Liver cirrhosis is associated with a myriad of complications including cardiac, renal, immune, and neurologic dysfunctions.[3] Patients with cirrhosis may also present with a diverse range of signs and symptoms that reflect the integral role that the liver has in the homeostasis of a multiple body functions.[4,5] There have been several studies which demonstrate that perioperative mortality is significantly higher in patients with cirrhosis undergoing surgery compared with the general population.[6] Cirrhotic patients with high Child-Pugh score, low albumin, poor nutritional status, poor renal and/or cardiac function have usually a higher mortality[7,8] among other cirrhotic patients. Many surgical procedures and its complications including wound infection, bleeding, length of study, and others parameters have been well studied in cirrhotic patients.[9] In the general population, the risks following appendectomy are as follows: surgical wound infection (4.0%), prolonged ileus (3.8%), deep wound infection (3.6%), systematic sepsis (1.2%), and prolonged bleeding requiring transfusion (0.4%).[9,10,11] There have been few, small-scale studies conducted to examine the complications and mortality rate associated with appendectomy in cirrhotic patients. The surgical removal of an inflamed appendix is the most common surgical emergency worldwide. Although it has been over 100 years since Reginald

Heber Fitz characterized the typical presentation and pathophysiology of appendicitis and appendectomy, appendicitis continues to present challenges for the surgeon today.[12] Appendectomies, in the United States, account for more than 1 million hospital days per year. Our study examined the mortality and complication rate associated with appendectomy in cirrhotic patients compared with the general population. The study has clearly shown that morality rate in cirrhotic patients is not higher than the general population and, therefore, should not be a contraindication for surgery.

## Methods

The 2010 National Inpatient Sample (NIS) was used. The NIS is the largest all-payer inpatient care database containing around 8 million hospital stays from about 1000 hospitals in the United States. These data are collected as part of the Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ). The NIS is designed to approximate a 20% sample of US non-Federal hospitals, including public hospitals and academic medical centers assigned by the American Hospital Association.

Each hospital record includes a unique patient identifier, demographic data, admission type, primary and secondary diagnosis and procedures, primary and secondary insurance payers, length of stay including hospital charges, and hospital characteristics. Hospital geographic region was subcategorized into Northeast, Midwest, West, and South. The control/ownership of the hospitals was classified as government non-Federal (public), private not-for-profit (voluntary), and private investor-owned (proprietary).

### *Case and outcome variable identifications*

The *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) diagnostic codes are used to capture all admissions in the NIS data set with appendectomy-related admission and has history of cirrhosis. *International Classification of Diseases, Ninth Revision* (*ICD-9*) code for laparoscopic appendectomy (4701) and ICD-9 code for cirrhosis (5710, 5712, 5713, 5715, 5716, and 5718) were used. The rest of the variables are already defined in the NIS data.

### *Statistical analysis and the study design*

The primary outcome of the study is to examine the difference in the morbidity and mortality of laparoscopic appendectomy in people with cirrhosis vs noncirrhotic patients. Inclusion criteria were all race and sex who are 18 years or older. Those who have laparoscopic appendectomy and have a history of liver cirrhosis were assigned to case group. An equal random number of appendectomy-related admissions and those who have no history of liver cirrhosis were selected and placed in the control group. Only laparoscopic appendectomy-related admission was included as it is the most commonly used procedure to remove the appendix these days. The procedure used in SPSS for selecting control group is called arbitrary random equivalent number. Case-control (appendectomy with history of cirrhosis vs appendectomy without cirrhosis) design is used.

**Table 1.** Demography.

| | *P* VALUE | NO CIRRHOSIS | HISTORY OF CIRRHOSIS |
|---|---|---|---|
| Mean age, y | .54 | 43.75 | 46.68 |
| Sex | | | |
| Male | .55 | 131 (34.7%) | 203 (54%) |
| Female | .65 | 247 (65.3%) | 173 (46%) |
| Total | | 378 (100%) | 376 (100%) |
| Race | | | |
| White | .05 | 313 (83.2%) | 238 (63.5%) |
| African American | .005 | 21 (5.6%) | 15 (4%) |
| Hispanic | .006 | 23 (6.4%) | 97 (26%) |
| Asian | .65 | 6 (1.7%) | 7 (2%) |
| Native American | | 0 (0.0%) | 4 (1%) |
| Others | | 11 (3.1%) | 12 (3.1%) |
| Total | | 378 (100%) | 376 (100%) |
| Mean length of stay | | 1.1 | 1.52 |

Data were analyzed using the IBM SPSS version 24 statistical software for Mac computer. Mean, percentages, and standard deviation of the mean were used to examine the demographic feature of the target population. Multivariate logistic regression statistical test is used to see whether there is any difference in mortality and morbidity in case vs control group (see Table 2). A confidence interval (CI) of 95% and *P* value less than .05 were determined to define the statistical difference between the 2 groups.

## Results

A total of 754 appendectomy-related admissions were identified—376 appendectomy-related admissions and history of cirrhosis (case group) and 378 admissions with appendectomy and no history of cirrhosis (control group). Of 754, 520 were white (73.5%), 34 black (4.8%), 115 Hispanic (16.2%), 13 Asians (1.8%), 4 Native American (0.6%), and others (3.1%). In all, 334 (44.3%) were men and 420 (55.7%) were women. The mean age was 43.75 years for the case group and 46.68 years for the control group (see Table 1).

Comparing cirrhotic with noncirrhotic group, the mean length of stay was 1.1 vs 1.52 days, inpatient mortality was 2 (0.5%) vs 1 (0.3%), ($P$ = .56, odds ratio [OR] = 2, 95% CI: 0.18-22.3), pneumonia 8 (2.1%) vs 3 (0.8%) ($P$ = .142,

**Table 2.** Logistic regression analysis of morbidities and mortalities.

| MORBIDITY AND MORTALITY | APPENDECTOMY AND CIRRHOSIS (379) | APPENDECTOMY AND NO CIRRHOSIS (378) | *P* VALUE | OR (95% CI) |
|---|---|---|---|---|
| Mortality | 2 (0.5%) | 1 (0.3%) | .56 | 2 (0.18-22.3) |
| Pneumonia | 8 (2.1%) | 3 (0.8%) | .142 | 2.717 (0.71-10.32) |
| Surgical site infection | 3 (0.8%) | 2 (0.5%) | .652 | 1.52 (0.25-9.10) |
| Urinary tract infection | 18 (4.8%) | 12 (3.2%) | .26 | 1.53 (0.72-3.22) |
| Postoperative bleeding | 3 (0.8%) | 2 (0.5%) | .65 | 1.51 (0.25-9.1) |
| Pulmonary thromboembolism | 1 (0.3%) | 0 (0.0%) | .94 | 0 (0.03-0.8) |
| *Clostridium difficile* infection | 1 (0.3%) | 0 (0.0%) | .99 | 0 (0.0-0.0) |
| Upper gastrointestinal bleeding | 3 (0.8%) | 1 (0.3%) | .332 | 3.02 (0.3-29) |

OR = 2.7, 95% CI: 2.7-10.32), surgical site infection 3 (0.8%) vs 2 (0.5%) ($P$ = .652, OR = 1.52, 95% CI: 0.25-9.10), urinary tract infection (UTI) 18 (4.8%) vs 12 (3.2%) ($P$ = .26, OR = 1.53, 95% CI: 0.72-3.22), postoperative bleeding 3 (0.8%) vs 2 (0.5%) ($P$ = .65, OR = 1.51, 95% CI: 0.25-9.1), pulmonary thromboembolism 1 (0.3%) vs 0 (0.0%) ($P$ = .94, OR = 0, 95% CI: 0.03-0.8), *Clostridium difficile* infection 1 (0.3%) vs 0 (0.0%) ($P$ = .99, OR = 0), upper gastrointestinal (GI) bleeding 3 (0.8%) vs 1 (0.3%) ($P$ = .332, OR = 3, 95% CI: 0.3-29) (Table 2).

## Discussion

The increase in the prevalence of the NASH and the chronic HCV infection both contribute to the increase in the incidence and prevalence of cirrhosis in the United States. Accompanying that increase, the physicians and hospitals will be exposed to more medically complicated cirrhotic patients in addition to emergencies and elective surgeries. Acute appendicitis is one of the most common surgical emergencies in United States and it occurs in 7% of the general population with an incidence of 1.1 cases per 1000 persons annually, whereas its incidence in cirrhotic population is not well studied.[9]

Appendectomy, laparoscopic approach or open laparotomy approach, is the standard of care in the management of patients with acute appendicitis and associated with low morbidity and mortality rate in the general population, whereas its morbidity and mortality in cirrhotic patients have yet to be sufficiently compiled. Although the nonsurgical approach with the administration of antibiotics is safer in the nonsurgically candidate patients, that approach was found to be associated with high rate of recurrence and peritonitis in an open-label randomized clinical study done in France by Vons et al[10] in a cohort of 243 patients. Very few studies examined the mortality and morbidity of appendectomy in cirrhosis. Our study is the largest study focusing on the appendectomy in cirrhotic patients and determining the risk of postoperative complications, including wound infection, pneumonia, UTI, *C difficile*–associated diarrhea (CDAD), GI bleeding, and length of stay in 376 patients, and comparing the result with noncirrhotic randomly selected controls.

Tsugawa et al[12] compared the laparoscopic appendectomy with open appendectomy in 40 cirrhotic patients and found less wound infection, less wound bleeding, and shorter hospital stay in the laparoscopic appendectomy group. Puggioni et al reported that the risk of wound infection was 1.6% in his meta-analysis of cirrhotic patients who had laparoscopic cholecystectomy. That low incidence was also reported by the study by Ziser et al, who reported that the risk of wound infection was low and representing 2.6% of his cohort. In our study, the risk of wound infection was lower than the published data and was not different from the noncirrhotic group (control group) with percentages of 0.8% and 0.5%, respectively ($P$ = .65).[13,14]

Ziser et al found that pneumonia was the most common postoperative complication in cirrhotic patients who undergone surgical procedure under anesthesia representing 8% of his cohort of 733 patients, whereas Georgiou et al found that the risk was higher in cirrhotic patients undergoing laparotomy operation in trauma patients with a percentage of 11%.[13,15] In contrast, our data suggest that the risk of pneumonia is less than the suggested data with a percentage of 2.1% of the total cohort and it was not statistically significant from the control group with $P$ value of .142.

Urinary tract infection represents 13% of all health care–associated infections in the United States and is associated with an increase in the mortality rate. Tsugawa et al reported that 4% of the patients in his cohort developed UTIs. In contrast, our data showed that the risk of UTI is higher than what Tsugawa et al have reported and it was higher than the noncirrhotic group too. The risk of UTI was 4.8% in the cirrhosis group and 3.2% in the control group ($P$ = 1.53).[12]

The risk of developing CDAD postoperatively in general population considered to be low and studies estimated the prevalence to be ranged between 0.5% and 1.2%, higher risk found in patients with hypoalbuminemia and immunosuppression.[16,17]

In cirrhotic population, the risk of CDAD is higher than noncirrhotic secondary to 3 reasons: first, the usage of antibiotics in preventing infection and improving mortality especially quinolone which is known to be associated with a high risk of CDAD.[18,19] Second, the use of proton pump inhibitor is more common in the cirrhotic population which is associated with high risk of developing CDAD.[20] Third, the frequent hospitalization carries high risk of developing CDAD.[21] Bajaj et al[22] found in his retrospective study that CDAD has higher mortality when compared with noncirrhotic patients. Our cohort showed that only 1 patient (0.3%) had CDAD during his hospitalization for the appendectomy and none found in the noncirrhotic group.

Bleeding, upper GI bleeding and postoperative bleeding, was reported by Ziser et al in their 733 cirrhotic patients. Ziser et al[13] found that the percentage of GI bleeding and surgical bleeding was 4.6% and 4.9%, respectively. Our cohort showed that the risk of bleeding following appendectomy was very low. The percentages of postoperative bleeding and upper GI bleeding were reported in our cohort as 0.8% and 0.8%, respectively.

The mortality rate in the general population is low and ranged between 1.8% and 1%, whereas the mortality rate in our cohort was low with percentages of 0.5% and 0.3%, respectively, and not statistically significant between the 2 groups.[23]

Although our data do not show the severity of the cirrhosis and the level of the impairment of the liver function due to the lack of the ability to calculate the Model For End-Stage Liver Disease (MELD score) and Child-Pugh score, the findings showed that the risk of complication is not different between the 2 groups. Such findings could be explained by the general improvement in the sterile techniques, new high technology devices, and the increase in the surgical laparoscopic experience. Our study had certain limitations in that the NIS is a retrospective database using administrative *ICD-9* codes, thus questioning the accuracy of coding procedures. Our data lack the information about the degree of cirrhosis and does not include MELD score or Child-Pugh score that is usually used to determine the severity of the disease. Our data do not include the synthetic function of the liver (albumin and international normalized ratio), which affects the postoperative course. The platelet number is not included in our study which could affect and correlate with the risk of bleeding in the cirrhotic patients. Finally, there could be also a clerical error involved as the database is taken from charts completed by humans, with human error, as well as completion of charts from many different institutions across the United States. Although several limitations may exist, we believe that these are counterbalanced by the large sample size and absence of reporting bias as in some publications from specialized centers or those with a financial interest.

## Conclusions

Appendectomy in cirrhotic population is a safe procedure and does not have mortality and morbidity differences from noncirrhotic population.

## Author Contributions

YA-AB and YA-AZ are the co authors of the manuscripts. Both helped in the design, and/or acquisition of data, and/or analysis, interpretation of data and writing the manuscripts. MF participated in drafting the article and revising it critically for important intellectual content. TN gave the final approval of the version to be submitted.

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